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(Concluded)

AN INJECTION STUDY OF UTERINE BLOOD VESSELS*

ROBERT L. FAULKNER, M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, University Hospitals and Western Reserve Medical School)

INJECTION studies of the blood vessels of the uterus are not new. Sampson¹ in 1913, injected the vessels of the surgical specimen with gelatin and studied the vascular pattern in cross sections and radiographically. He learned that the uterine veins contain no valves and are injectable. Since then the arteries, particularly, of the myometrium and endometrium have been studied by Barthelmez² from 1930 to 1941, by Jones and Brewer³ in 1939, and others. In the monkey, Daron⁴ in 1936, made a valuable contribution to our knowledge of the arteries of the endometrium by injecting mercuric sulfide into the vascular system during anesthesia. By immediately freezing the uterus in situ upon opening the abdomen, it was possible to study the vessels of the endometrium practically as they exist during life.

While injecting the arteries and veins of the myomatous uterus⁵ with synthetic liquid latex, or Neoprene, it became apparent that good gross injections of the intrinsic vessels of the uterus were obtained. Therefore, injections were carried out on uteri removed for one cause or another at different phases of the menstrual cycle and on some bleeding uteri, especially those which contained only small or no demonstrable myomas. Over fifty specimens have now been injected for the study of the intrinsic vessels.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

Neoprene as an injection compound is easy to use, and this is important for the routine injection of suitable surgical specimens. It needs only to be filtered to be ready to use which is quite different from the commonly used gelatin which has to be prepared, kept free from mold, melted each time for use, and necessitates warming and chilling of the specimen before and after injection.

Injection of the blood vessels in a uterus of normal size is more difficult than the injection of those of a uterus containing myomas. There are two reasons for this: 1. The uterine vessels are smaller and less easily cannulated for injection; 2. The injection necessarily is the injection of end arteries and their emptying veins instead of the injection of a vascular arc as in most myomas.

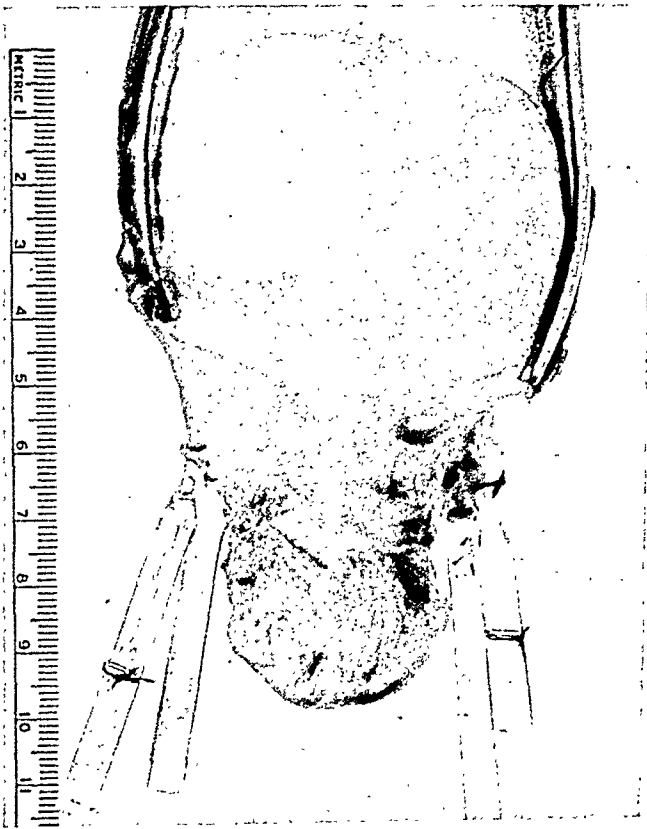


Fig. 1.—Uterus ready for injection. Black threads are on the venous cannulas.

In this study the method of injection was standardized as rigidly as possible. Throughout, the washing of the specimen was done in the same manner, the injection pressures used were always the same, the time of injection postoperatively was always the same, and all injections were done at room temperature.

All patients whose uteri were utilized were personally interviewed and their menstrual dates and habits carefully tabulated with full notation, also, of age, parity, and of any recent abnormal bleeding. Since the great majority of the specimens were for technical reasons of satisfac-

tory injection removed personally, this was no cursory inquiry. Hysterectomy was done carefully without traction sutures or clamps when possible. In some instances, a single traction suture was placed through the vertex of the uterus but used as little as possible.

Injection Method

Small glass cannulas (Fig. 1) were inserted into both uterine arteries and veins of the freshly removed specimen and at low pressure the blood washed out by connection to the arterial cannulas with a minimum amount of normal salt solution to produce blanching of the specimen. The uterus was then covered and put in the refrigerator over night, all leaking vessels having been ligated. Injection was done the next day, or twenty-four hours after removal of the uterus. All gross edema produced by the washing had by that time disappeared.



Fig. 2.—Corrosion cast of uterus showing black venous mass and uterine arteries with arcuate branches. Uterine veins cut away. Fundal branch toward top on either side. (From *AM. J. OBST. & GYNEC.* 47: 185-197, 1944.)

Two forms of synthetic liquid latex were used: 1. A red suspension for arteries with a granule size of about 0.4 microns; 2. The other, a suspension containing a blue-black pigment for veins with a granule size of about 2 microns. The exact pigments contained in these preparations are not known, since they are proprietary injection compounds.* Lieb⁶ found that they are satisfactory in obtaining a high percentage of glomerular injections in the kidney, and that in a general way, the granules go over into but not through the capillary bed.

On being brought back to room temperature, the arteries were injected with red neoprene from a simple pressure bottle set between 180 and 200 mm. of mercury. When the arteries were filled, there was no further flow. Black neoprene was then introduced into the veins at

*American Anode Inc., Akron, Ohio.

a pressure of 160 mm. of mercury. Filling of the veins produced a tense, swollen, and uniformly black uterus. Gentle massage of the specimen was carried out during venous injection to fill all the sinusoids. After removal of the cannulas, the vessels were tied and the specimen placed in 5 per cent formaldehyde strongly acidified with acetic acid. Any acid promptly sets this injection compound.

After thorough fixation, the uterus was bisected longitudinally and anteroposteriorly with a long sharp knife.

Neoprene lends itself to the preparation of multicolored corrosion specimens (Fig. 2). This preparation is made by eating off all the flesh with commercial hydrochloric acid leaving only the injected cast of



Fig. 3.—Arterial pattern of uterus. Spalteholz cleared preparation. One small myoma in uterine wall. Cervix does not inject in a surgical specimen. (From AM. J. OBST. & GYNEC. 47: 185-197, 1944.)

the circulation. The cervix does not inject in a surgical specimen because its vessels are stripped off during removal of the uterus. The uterine arteries with their arcuate branches to the front and back of the uterus are obvious. The uterine veins have been cut away. A large branch of the uterine artery usually goes on over the fundus. The large bulk of the venous sinusoids which retain the contour and almost the complete size of the original specimen is evident.

The internal arterial pattern of the uterus may be seen in Spalteholz cleared specimens. The black pigment in neoprene will stand the clearing process in benzol and wintergreen oil (Fig. 3). The rich peripheral circulation of the uterus may be seen. Through these anastomoses one

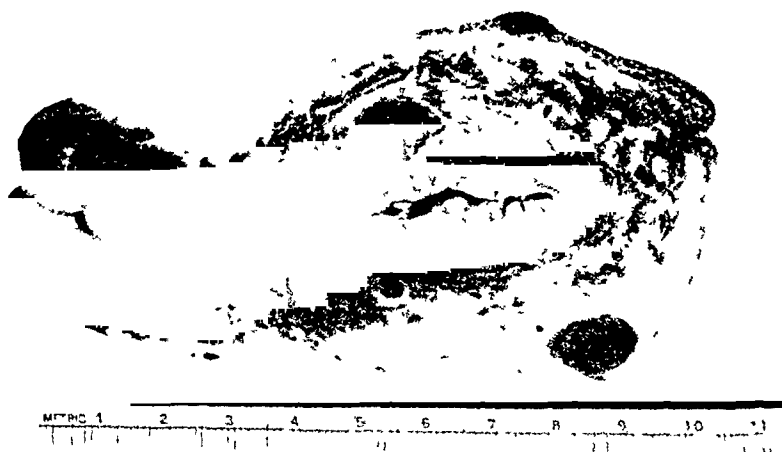


Fig. 4.

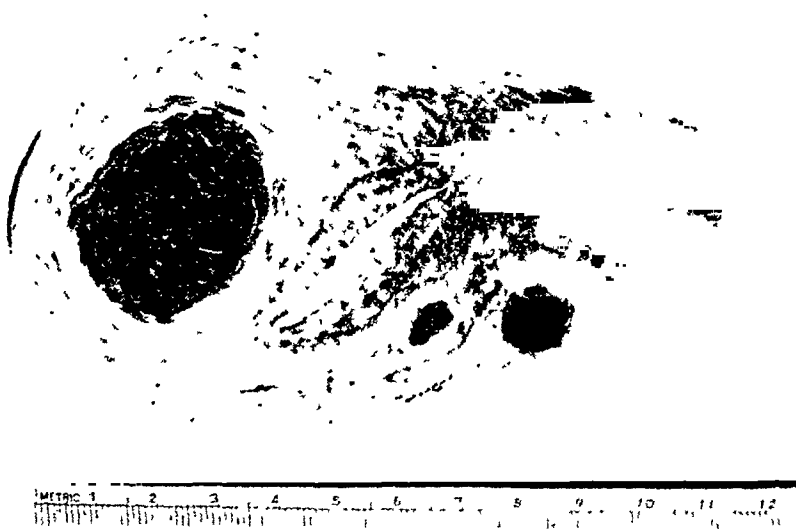


Fig. 7

Fig. 4.—Injection of uterus removed seventh day of menstrual cycle. Aged 45. Para iii. Small myomas. Periods normal. Zone of uninjectability about uterine cavity.

Fig. 7.—Beginning of menstrual flow. Aged 38. Para i. Escape of venous injection mass into uterine cavity.

uterine artery communicates so freely with the other. The pattern of the radial arteries all pointing toward the uterine cavity is always almost diagrammatic unless distorted by myomas.

Neoprene in common with other colloids does not penetrate the terminal branches of the radial arteries. They are filled normally only up into the inner quarter of the myometrium. The endometrium is not injected. Daron believed that in addition to a contraction cone active during life, that there is also an anatomical narrowness of arteries in the submucosal zone before they enlarge again to those of the endometrium. Injection experience with neoprene would seem to confirm this opinion.

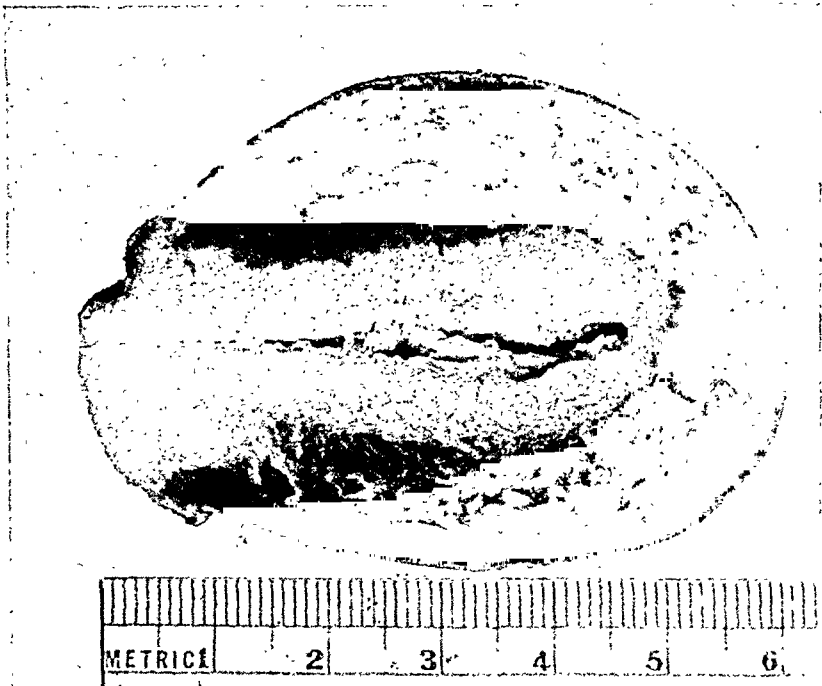


Fig. 5.—Fourteenth day of cycle. Aged 28. Para i. Slightly more injectability of submucosal zone.

Therefore, it is particularly the veins of the uterus as they may be an index to blood supply that are studied with neoprene. It is true that the arteries of the endometrium seem to be important in explaining the now well-known rhythmic blushing and blanching of the endometrium in menstruation, and also probably explains its shedding, but it has never been proved successfully that the source of menstrual blood may not be venous reflux in large measure.

Sampson observed in many specimens an uninjectable zone about the uterine cavity except in uteri which were bleeding, about to bleed, or had recently been bleeding. In specimens carefully arranged as to menstrual dates and not containing myomas which might interfere with the picture, it would seem that this zone of uninjectability is an almost constant finding postmenstrually up to approximately the time of ovulation (Figs. 4 and 5). After that there is increasing venous in-

jectability of this area with uniform and almost complete entrance of the injection mass as menstruation approaches (Figs. 6 and 7).

Near the end of menstruation (Fig. 8) in a limited number of specimens injected at this time, there is a return of the uninjectable zone except opposite areas where shedding of the endometrium is incomplete. The same picture of patchy or irregular injectability is seen in other uteri with abnormal bleeding (Fig. 9).

With the aid of Dr. Normand L. Hoerr, Professor of Anatomy, efforts were made to prove the postmenstrual ischemic zone an injection artefact.



Fig. 6.—Twenty-fifth day of cycle. Aged 30. Para i. Uniform injectability of sub-mucosal zone.

Obviously all tissues, particularly veins and smooth muscle, should be devitalized after twenty-four hours. To make sure, however, that the time of injection made no difference, several specimens were injected as late as four or five days after operation. If the uterus was postmenstrual, the same uninjectable zone was observed. Nitrite solutions were perfused through the arteries. Specimens so treated did not seem to be altered in their injectability. The possibility of connective tissue swelling during the washing process with clamping off of veins was considered. Several specimens were injected without washing. These were the poorest of all. An occasional specimen was injected only through the arteries in an effort to see if veins in the uninjectable zone would be filled with blood. No filling of the veins by this method was proved. Briefly, nothing to date has succeeded in altering

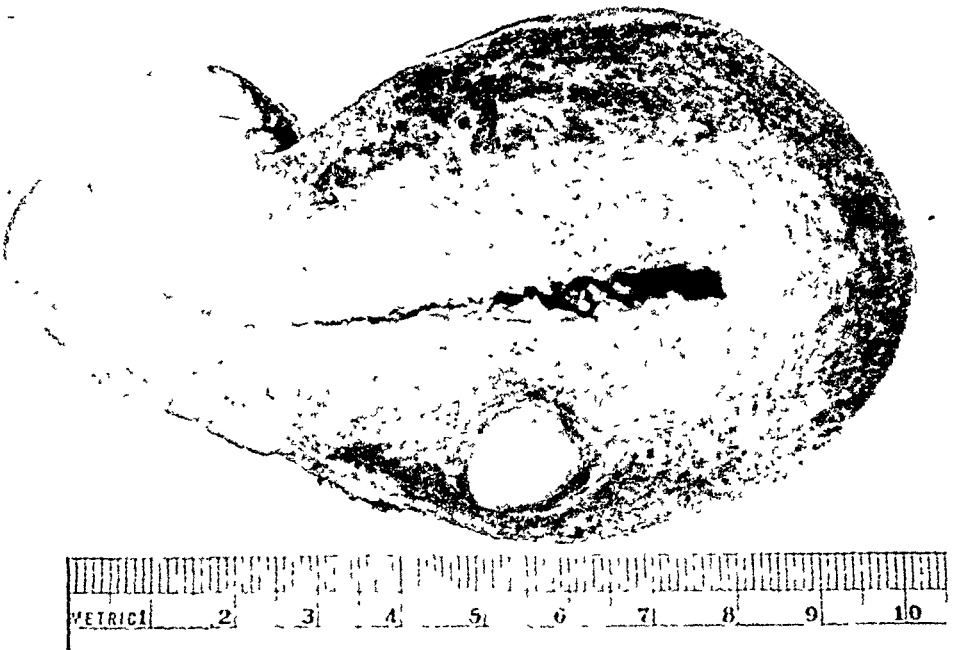


Fig. 8.—Third day of usual four-day period. Aged 44. Para ii. Return of uninjectable zone except at points opposite small myoma where endometrium remains to be shed.

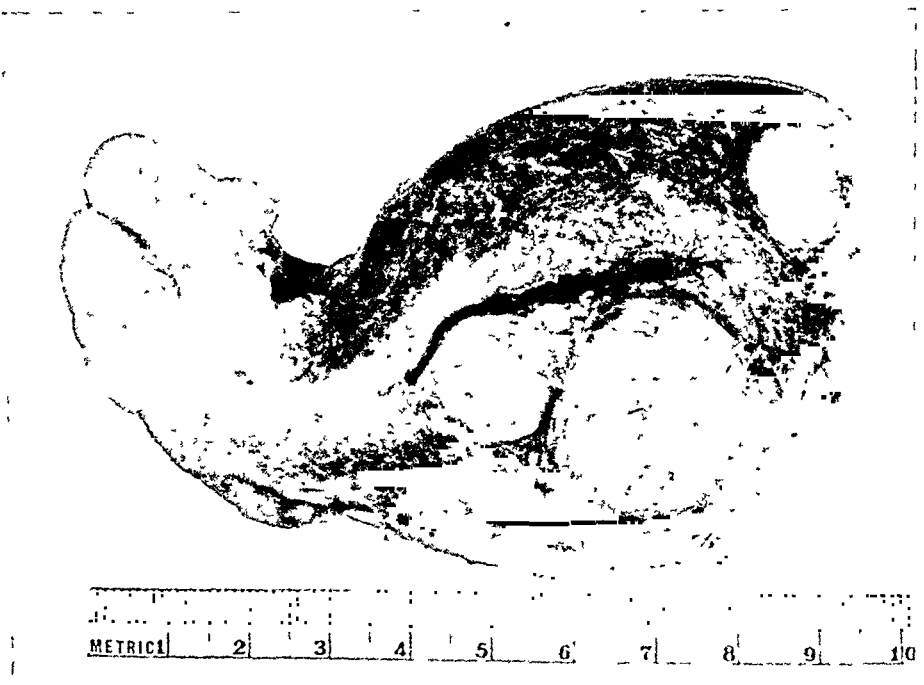


Fig. 9.—Uterus removed twelfth day of bleeding. Aged 32. Para 0. Escape of venous mass through middle portion of uterus with less injectability in vertex and lower uterine cavity.

the general picture of uninjectability in the submucosa of the endometrium.

This region was studied with special stains microscopically. There is no obvious increase in connective tissue postmenstrually that can be seen in Masson's stain. The only thing that is regularly apparent is a definite increased compactness of the musculature in this region. Premenstrually, the zone becomes loose and spongy and is injectable with the greatest of ease.

Summary and Conclusions

In the uterus carefully removed at surgical operation and the vessels injected with synthetic liquid latex with a standardized technique, the presence under ordinary conditions postmenstrually of an uninjectable zone surrounding the uterine cavity as observed by Sampson over thirty years ago is observed again. Attempts were made without success to prove this zone an injection artefact. Morphologically, no change in the uterine wall in this zone was recognized except an increased compactness of uterine musculature. This region, after the period, resembles the myoma somewhat in its manner of injection. In the premenstrual uterus, this zone becomes spongy and is injectable. In some specimens with irregular uterine bleeding, there may not be uniform injectability of the submucosa but a localized entrance of the injection mass here and there to the endometrium.

Since the type of endometrium has been rather conclusively found to have little connection with the fact of uterine bleeding, it would seem a legitimate effort to learn more if possible of the physiology of the uninjectable zone surrounding the uterine cavity.

Grateful acknowledgment is made of the technical advice of Miss E. Lieb in making these injections, to Dr. Normand L. Hoerr for critical analysis of the material, and to the Department of Pathology for the colored illustrations.

References

1. Sampson, J. A.: *Surg., Gynec. & Obst.* 16: 144, 1913. *Ibid.* 18: 587, 1914.
2. Barthelmez, G. W.: *J. A. M. A.* 116: 702, 1941.
3. Jones, H. O., and Brewer, J. I.: *AM. J. OBST. & GYNEC.* 38: 839, 1939.
4. Daron, G. H.: *Am. J. Anat.* 58: 349, 1936.
5. Faulkner, R. L.: *AM. J. OBST. & GYNEC.* 47: 185-197, 1944.
6. Lieb, E.: *J. Tech. Methods* 20: 48, 1940.

Discussion

DR. WILLIAM E. STUDDIFORD, New York, N. Y.—Dr. Faulkner has presented a simple and efficient method of demonstrating the intrinsic arterial and venous systems of the uterus. Synthetic latex appears to have definite advantages over the more difficult gelatin mass formerly utilized in such studies.

His study of relatively normal uteri injected in this fashion has yielded results, which conform closely with those obtained by Sampson in a report presented before this Society over thirty years ago. In the older report the same zone of low injectability was noted adjacent to the endometrium, although the alteration of this zone in the premenstrual phases was not stressed. Both of these reports have

suggested that this zone of the myometrium plays an important part in regulating the quantity of the menstrual flow.

This study strikes at the fundamentals of a most bothersome clinical problem. While much has been learned of the physiology of the menstrual cycle in recent years, particularly in regard to the growth and development of the endometrium under hormonal stimulation, and its breakdown following the withdrawal of such stimulation, this knowledge has proved to be of no value in the treatment of the patient who suffers from prolonged and profuse menstruation from a uterus which otherwise appears quite normal.

Studies of the endometrium obtained from these patients usually show no pathologic change. It is reasonable to suppose that the fundamental defect in many of them lies in the myometrium. Dr. Faulkner has demonstrated the area in which this defect may lie. Further studies of the myometrial relationship to menstrual bleeding may yield more constructive results.

Has Dr. Faulkner made any injection studies in uteri containing an early pregnancy? In several such specimens, containing pregnancies ranging from twenty-six to forty-four days of age, sections of the myometrium showed a pronounced zone of edema and vasodilatation beneath the serosa in the area supplied by the peripheral branches of the arcuate arteries. The changes suggest a zone of pronounced vascular disturbance in the outer third of the myometrium during the early months of pregnancy. They are not present in the inner two-thirds of the myometrium.

DR. FAULKNER (closing).—I desire to state that up to the present time no studies on pregnant uteri have been made.

RELATIONSHIP OF GLYCOGEN TO PROBLEMS OF STERILITY AND OVULAR LIFE*

EDWARD C. HUGHES, M.D., SYRACUSE, N. Y.

THE process of ovulation, fertilization and housing of the growing embryo is the important biologic function of the female species. The satisfactory maintenance of these processes depends upon the intricate function of the various endocrine glands, the metabolism of essential materials, and the effect of hormones and enzymes. There is no doubt that nature's most complex problem is to furnish ever increasing amounts of foodstuff, not only to the sperm after it enters the female generative tract, but particularly to the ovum after it leaves the Graafian follicle, is fertilized and implants itself on the surface of the endometrium. Essential nutriment for these vital cells include many substances, particularly oxygen and carbohydrates. Glucose has been found to increase in amount in the early fertilized avian egg and the eggs of lower mammals. An increased utilization of this sugar in human beings may be a phylogenetic remnant from these lower forms. The problem of providing these materials is difficult during the early period of implantation, before the embryo establishes a close intimacy with the mother by placental formation and growth. It is during these days of nidation that many observers have stated that the trophoblast lives almost exclusively on glucose and oxygen. This fact probably explains the presence of glycogen, the storage product of glucose, in such abundance in all parts of the reproductive tract, and leads to this discussion concerning the importance of this material to satisfactory nidation or ovular life.

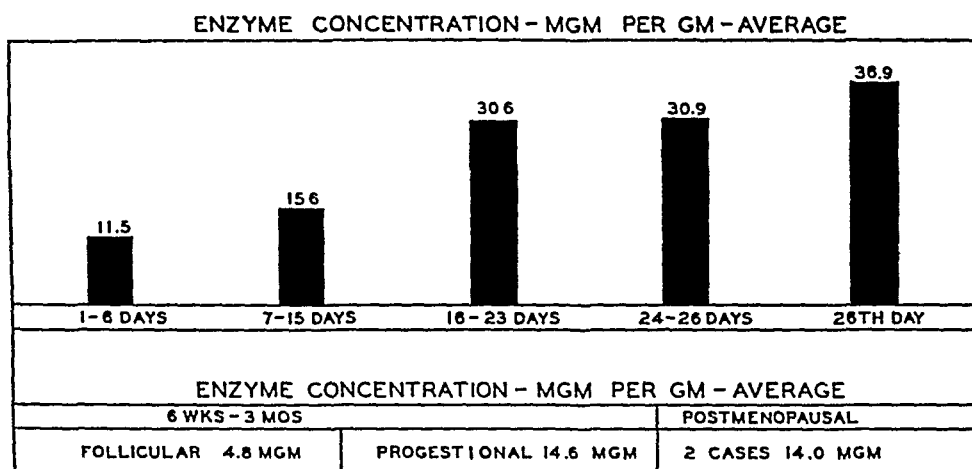
Distribution of Glycogen in the Reproductive Tract

In normal individuals, glycogen seems to be present in all the tissues with which the ovum comes in contact. It is found in the cells of the cumulus oophorus while the egg is still in the Graafian follicle. It is secreted by the epithelial cells of the Fallopian tubes. It is produced in the endometrium of the uterus in increasing amounts after ovulation and fertilization. It is during the early days of implantation that some intermediate substance of low molecular weight such as glucose and oxygen must be provided by the endometrial glands to furnish nutriment which is easily and readily assimilated. However, inasmuch as glucose cannot be stored as such, it must be derived from glycogen. One can thus feel that glycogen is stored in the endome-

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

trium in anticipation of fertilization whereby in the usual chemical manner, sugar is made available for ovular usage. This chemical process is probably similar to that which goes on in the other organs of the body where conversion to glycogen and storage occurs. This glycogenesis and glycogenolysis must go on in the endometrium in the same manner, involving the presence of an enzyme or possibly by enzymes.

The endometrium has been examined for enzymes previously by Reynolds and others. They have concluded that there perhaps are several present. In this study, sections of endometria have been removed by the biopsy curette, and have been studied for the presence of an enzyme responsible for the glycogen hydrolysis. The subjects from whom these biopsies were removed were fifty normal women, who had given normal menstrual histories. The method, as worked out by Dr. Robert K. Brewer, Professor of Chemistry, College of Medicine, Syracuse University, is as follows:



Method of Enzyme Determination

Samples of endometrial tissue removed by curette were carefully wiped with filter paper, in an attempt to remove as much as possible of the adherent mucus, and then the samples were transferred to weighed tubes and again weighed. A mixture of 25 per cent glycerin in normal saline at pH 5.0 was added, and the sample extracted for 24 hours at 38° C. with occasional shaking. Aliquot portions of the extract were treated with ten volumes of 95 per cent alcohol, and the precipitated enzyme thrown down in a centrifuge tube. After thorough draining, the enzyme was dissolved in a pure glycogen solution and incubated at 38° C. for 24 hours. The reducing substance was then determined by Benedict's blood sugar method, calculated as glucose, and reported as milligrams of reducing sugar per gram of tissue. Blanks were run on all reagents used as well as on heated controls to give proof that the reducing substance formed was the result of enzyme action on the pure glycogen in solution.

The only claim advanced for the value of the figures obtained is that by doing 147 analyses by the same method, using the same reagents, we obtained results which we consider to be of value for comparative purposes.

The average amounts of enzyme seem to vary according to the menstrual cycle. These are illustrated in the following:

Days	1 to 6	7 to 15	16 to 23	24 to 26	26
	11.5	15.6	30.6	30.9	36.9 mg. per gram

It was also observed that as far as we could determine, the hydrolysis of glycogen by this enzyme did not pass to glucose but to a di- or tri-saccharide. The enzyme was also found in larger amounts in mucous secretion of the endometrium than in the tissue itself. It was interesting to note that determinations made upon women in the six-week to three-month period post partum, and postmenopausal women were definitely lower than normal. These averages were as follows:

Sixth week to three months, in the follicular phase—4.8 mg.

Progestional phase—14.6 mg.

Postmenstrual women—14.0 mg.

Although it seemed as if the enzyme production varied quantitatively with the phase of the cycle, it was found necessary that the endometrium be studied carefully to correlate the amounts of enzyme with the location and quantities of glycogen present in the various phases of the cycle. Therefore, each biopsy of the endometrium that was obtained for enzyme determination was also stained for glycogen. These sections were stained by Best carmine technique.

The Distribution of Glycogen in the Endometrium

The distribution of glycogen in the endometrium seemed to be important, and seemed to follow a constant sequence of events in the normal cases, according to the phase of the cycle. Glucose was brought to stroma of the endometrium by the arterioles, where dehydration to glycogen apparently started. This occurred about the end of the first week of the follicular phase, and the glycogen appeared as small granules sparsely scattered about the base of the endometrial glands. (Fig. 1.) Dehydration continued during the second week, followed by beginning accumulation at the base of the glandular epithelial cells. (Fig. 2.) The nuclei of these cells were pushed upward to the mid-zone of the cell. (Fig. 3.) At the end of the second week, glycogen continued to be stored in granular form until after ovulation, when it was released from the epithelial cells into the lumen of the glands and onto the surface of the endometrium. (Fig. 4.) The periphery of the epithelial cells became frayed and ragged after glycogen was released. The glycogen was then hydrolized by enzymatic action into a reducing sugar.

Relationship of Glycogen and Enzyme Concentration to Sterility

GROUP I

66 PATIENTS AVE AGE 30 YRS

The first group consisted of 66^b women, who were found to have a normal endometrial pattern, with normal distribution and amount of glycogen. (Fig. 5.) The cause of the sterility was from some pelvic pathology, or male impotency. After correction of the local difficulties, pregnancy resulted in 26 patients. The following treatments were carried out:


1. Retroversion corrected with pessary in 15 cases, followed by pregnancy in 11 patients.
2. Cervical erosion and stenosis were treated in 2 cases with resulting pregnancies.

3. Tubal patency tests were done on all patients. Seventeen patients were found to have tubal obstruction. Five of these patients conceived after treatment.

4. Eight patients conceived after treatment of other conditions that were present, such as erosion of the cervix and trichomonas vaginitis.

Seventeen patients of this group had enzyme determinations done upon the endometrium. The average was 30.5 mg. per gram, which is considered normal.

The second group of patients consisted of 27 women, in whom the endometrium failed to proceed farther than the proliferative phase, and the glycogen was absent or present in only small quantities. (Fig. 6.) Enzyme determination in 7 patients was under normal, averaging 16.4 mg. per gram. These patients were treated with all the various gonad-stimulating hormones. The results were unsatisfactory. Ovulation and pregnancy occurred in only 1 patient, the fetus was born a Mongolian idiot.

27 PATIENTS				GROUP II		AVE. AGE 28 YRS				
ENDOMETRIUM		ENZYME CONC.		MENSTRUAL HIST.		LOCAL PATHOLOGY		BMR	MALE	
PHASE	GLYCOGEN	36.9 MGM/GM				UTERUS - NORMAL		12		
PROLIF- ERATIVE	NONE 16			28 DAYS	6	SMALL	10	ABOVE,		
	SLIGHT 11			24-28 DAYS	4	RETRO.	5	13		
27		5WKS-2 YRS	17	TUMORS	0					
RELEASE	0					OVARIES - TUMORS		2	NORMAL,	2
STROMA	3					TUBES - CLOSURE		1	0	
CELLS	8								BELOW,	
									14	
NORMAL 7 PTS										
RESULTS										
1 PREGNANCY - MONGOLISM										

The third group, consisting of 47 patients did not seem to present a normal endometrial pattern, the glycogen distribution was irregular, and the enzyme content was markedly below normal. The phase of the cycle proceeded to the early secretory phase in 31 patients, but did not correspond to the twenty-sixth day of the cycle. (Fig. 7.) The glycogen was not released from the cells in some cases, and in others was only partially metabolized. In the other 16 patients, the endometrium was spotty, in some areas progressing to the early secretory, and in other portions to the late secretory phase. The glycogen was partly released in some, or retained in the stroma about the glands in others. (Fig. 8.) The enzyme production was again below par, averaging 15.5 mg. per gram in 16 patients.

This group, inasmuch as they showed comparatively little pathologic findings in the pelvic organs, but showed disturbed menstrual function and abnormal endometrial patterns, was classified as endocrine problems, and was treated with this in mind with the following results:

1. Eight patients in the lower level of metabolism were treated with thyroid extract, and 4 pregnancies resulted.

Fig. 1.—Early proliferative phase with several granules of glycogen staining red at base of the epithelial cells.

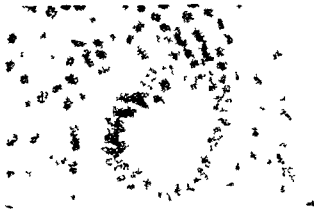


Fig. 2.—Nuclei pushed to midportion of cell by glycogen granules.

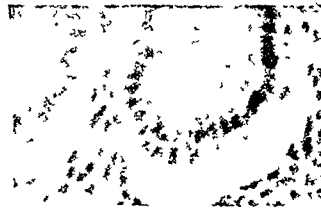


Fig. 3.—Early secretory phase with some glycogen release into lumen of gland.

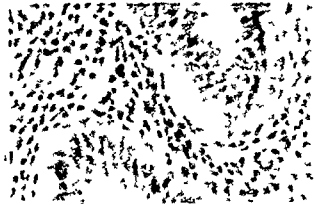


Fig. 4.—Glycogen granules released into lumen of gland. Late secretory phase.

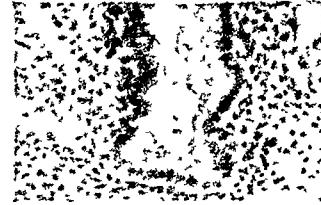


Fig. 5.—Normal endometrium with glycogen release in secretory phase.



Fig. 6.—Endometrium remains in the proliferative phase without glycogen.



Fig. 7.—Late proliferative phase with partial glycogen metabolism.



Fig. 8.—Glycogen retained in the stroma. Glandular epithelium is devoid of glycogen. Poor metabolism of glycogen.



Fig. 9.—Biopsy taken after pregnancy while ovum is still in tube. Large amount of glycogen in lumen of glands.

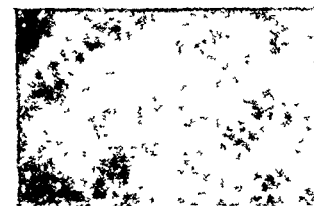


Fig. 10.—Pregnancy—large amount of glycogen.



Fig. 11.—Endometrial gland with glycogen present in glandular epithelium. Decidual cells with glycogen granules.

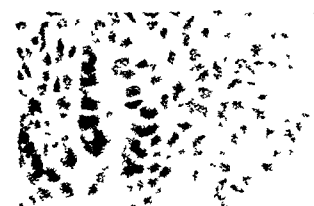


Fig. 12.—Chorionic villus surrounded by decidual cells containing glycogen granules.



2. Sixteen patients were treated with an estrogen, and 10 pregnancies resulted.

3. Sixteen patients were treated with a gonadotropic hormone, and 6 pregnancies resulted.

4. Two patients conceived following the endometrial biopsy, and 2 conceived without treatment.

GROUP III

47 PATIENTS		AVE AGE 29 YRS			
ENDOMETRIUM	ENZYME CONC	MENSTRUAL HIST.	LOCAL PATHOLOGY	BMR	MALE
PHASE SECRETORY 31	GLYCOGEN RELEASE 9	28 DAYS 15	UTERUS-NORMAL 26		
		21-28 DAYS 4	SMALL RETRO TUMORS 14	ABOVE, 22	
IRREG SECRETORY 16	STROMA S1 RELEASE 9 29	28-6 MOS. 28	OVARIES-NORMAL 47	NORMAL, 0	3
		SCANTY 2-3 DA. 21 NORMAL 4-5 DA. 16 MORE 5-10 DAYS 10	TUBES - NORMAL 47	BELOW, 25	
RESULTS - 24 PREGNANCIES					
	THYROID	ESTROGEN	GONADOTROPHIC	NONE	
PATIENTS TREATED	8	17	16	6	
PREGNANCIES	4	10	6	4 (2 PTS AFTER BIOPSY)	

The Relationship of Glycogen and Enzymes to Pregnancy and Spontaneous Abortion

While the metabolism of glycogen seems to be an integral part in the cyclic changes that occur in the endometrium in normal and abnormal cases, its continual and increased output seems particularly necessary after fertilization takes place.

Claude Bernard, in 1858, and later Chapman, found that glycogen was in abundance in the maternal portion of early placentas. Four endometrial biopsies obtained accidentally upon the twenty-sixth day of the cycle, after fertilization had occurred but while the ovum was still in the tube, revealed larger amounts of glycogen than usual in the epithelial cells and in the glands. (Figs. 9, 10.) Incidentally, these patients did not abort. Also, tissue removed for therapeutic abortion in the second month of pregnancy showed large granules of glycogen in the decidua and endometrial glands. (Figs. 11, 12.)

These demands for larger amounts of glycogen result in increased metabolism, involving more enzyme production, and greater supply of sugar to the endometrium. Failure of the endocrine system to provide this stimulation, with resulting lack of these materials ends in the death of the early embryo. It was interesting to note the frequency of spontaneous abortion in the three groups of patients just discussed. The incidence as obtained from their past histories was as follows: Fifteen women had a total of twenty-three miscarriages. The second group, where pregnancies were infrequent and enzyme con-

centration was low, five women had nine abortions. In the third group, in whom the glycogen distribution was abnormal, phase retarded and enzyme concentration low, twenty-six women had fifty-eight spontaneous abortions.

This would lead us to believe that when the glycogen metabolism is not complete, as shown in the third group of patients, the opportunities for ovum survival are not good. Microscopic studies were made upon the products of conception and curettings in some of these cases, and they showed early ovular death with necrosis and infiltration of leucocytes in the decidua.

INCIDENCE OF SPONTANEOUS ABORTION

	GROUP I, 66 PATIENTS	GROUP II, 27 PATIENTS	GROUP III, 47 PATIENTS
ENDOMETRIUM	NORMAL	ABNORMAL	ABNORMAL
ENZYME CONCENTRATION	30.5 MGM	16.6 MGM	15.5 MGM
SPONT ABORTION	15 WOMEN - TOTAL 23 26.6 %	5 WOMEN - TOTAL 9 18.5 %	26 WOMEN - TOTAL 58 55.3 %

Discussion

In discussing the importance of glycogen to these vital processes several opinions were formulated. Ovulation probably does not occur when the endometrium remains in the follicular phase, the glycogen is absent or diminished and the enzyme production low. This picture was exemplified in Group II. Opportunities for pregnancy in these individuals are few even after hormonal stimulation.

Individuals, in whom the endometrium proceeds to the progestational phase, possess relatively larger amounts of glycogen but still have a low enzyme output, conceive without difficulty; however, the chances of survival of the ovum are not good and spontaneous abortion results. These conditions were found in Group III. These women, however, were more amenable to treatment but the therapy should be instituted prior to pregnancy and during the early days of gestation. Ten patients in this series were treated as follows: Small doses of estrogen were given before pregnancy to improve glycogen and enzyme production as shown by endometrial biopsies and enzyme determination. After pregnancy occurred, combined treatment of small doses of estrogen and progestin were prescribed during the first trimester and early part of the second trimester. These women had never before carried beyond the fourth month, but after treatment proceeded uneventfully to term.

Summary

Several thoughts are brought to mind in attempting to summarize these findings.

1. A better understanding of the many chemical changes in the endometrium should be attempted.

2. Glycogen is an important material of the endometrium, and its metabolism is probably influenced by the ovarian hormones as previously described by Overhauser and Nelson.

3. Also, the glycolysis that occurs in this location may be associated with the metabolism of estrogen and progesterin in the endometrium itself.

4. There has been no proof that the progestational increase in amounts of glycogen and its enzyme is not associated with a general bodily increase.

5. The satisfactory metabolism of glycogen is necessary for ovulation and ovular life.

I wish to express my gratitude to Dr. N. P. Sears who has studied and diagnosed each biopsy sample.

Discussion

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—All of Dr. Hughes' material was sent to my laboratory and one technician prepared it. The glycogen stains were studied carefully and many types were tried before we were convinced of the properties of the stain. At first identical pieces of tissue were put through hematoxylin and eosin stains in addition to the glycogen-stained specimen. The slides were presented to me more or less as unknowns, so that I could identify the phase of the cycle and then follow the location of the glycogen granules in the tissue. I then went over the history of the case as found in the patient's record to look for any discrepancies from the normal. Some patients in the twenty-fifth or twenty-sixth day of the cycle showed some secretory areas highly developed and others poorly developed. The presence of glycogen coincided most of the time with the histology, but when there was a variation, the glycogen seemed to me more accurate. Dr. Hughes then took my reports without any comments on my part, except mention of the abnormalities, and studied the clinical factors along with the laboratory findings.

There is in this subject something of extreme general interest. We are at present in a phase in which we try to explain most functional derangements on a hormone basis, but the hormones have not solved all of our problems. I wonder if we will not be able to use the concept here presented to determine why so many women have long periods of amenorrhea, and others irregular and profuse bleeding without showing any pathological lesion, nor responding to hormone therapy. Some new studies on the metabolism of the sugars may be evolved which will make it possible to change the sugar metabolism and thereby bring about a better glycogen balance which, in turn, will correct the physiology of the childbearing organs.

DR. EMIL NOVAK, BALTIMORE, MD.—We may now have to add another to the already numerous procedures often indicated in the study of sterility. The fact that glycogen undoubtedly plays an important part in the nutrition of the egg before it implants itself in the endometrium makes it seem probable that it plays a similar role in the early postnidation phase. After the egg is thrown off from the ovary, a considerable number of days elapse before it takes root in the uterus. During this time, this single cell floats in space, so to speak, and yet if fertilized it lives and thrives. Where does it get its nutrition?

When it leaves the ovary it, figuratively speaking, packs a lunch box for itself, since with it go many adhering cells of the cumulus oophorus which will be assimilated by the egg, whose cytoplasm probably contains only a minimum of

nutritional granules in itself. During its transit through the tube, the egg may receive additional nutriment from the glycogen-rich cytoplasmic and nuclear extrusion of the secretory cells of the tube wall.

Even when it reaches the uterus, it does not at once implant itself, and during this loitering phase, it is further nourished by the glycogen-rich secretion of the uterine glands. In some animals, like the horse, this secretion is almost milky in its nutritional value, and has indeed been spoken of as "uterine milk." Still later the egg, in the process of implantation, benevolently assimilates the cells of the endometrium before it finally taps the maternal vessels for a more permanent source of nutrition.

The maternal decidua likewise is rich in glycogen, and it would appear from the studies of Zondek, and those reported today by Dr. Hughes, that the presence of this glycogen is important and perhaps essential for the implantation of the egg. Zondek described a glycopenia of the endometrium as associated with some cases of sterility, even when the endometrium shows a typical progesterational picture histologically.

In other words, it is hazardous here, as in so many other fields, to use mere morphological changes as a criterion of the functional status of a tissue. For example, even an actively mobile spermatozoon may be incapable of fertilizing an egg. Conversely, the mere fact that endometrial biopsy demonstrates that an egg has been thrown off does not justify us in assuming that the egg is a fertilizable one. To confuse the problem still more, we now must suspect that even if the egg is fertilized, it may meet with an unfavorable reception in the endometrium as a result of such factors as glycogen deficiency.

Since we know comparatively little as yet as to the endocrine or other mechanisms involved in these factors, we cannot attack them with any very intelligent corrective measures, but the mere recognition that they exist will help us to explain some of our sterility cases, and will spur investigators to further efforts to increase our knowledge on these points.

DR. KARL MARTZLOFF, PORTLAND, ORE.—I would like to ask Dr. Hughes just how he obtained his endometrial tissue for biopsy; whether samples were taken from the entire intrauterine cavity, or from just one or the other wall. It has been our experience that biopsies obtained from one point in the uterine cavity are an unreliable index as to the status of the endometrium, and that if one wishes to have a fair index it requires a sample from all walls of the cavity. We find that domestically manufactured carmine is an unsatisfactory substance and we have to use Grüber's carmine for our glycogen stains.

DR. HUGHES (closing).—Replying to Dr. Martzloff's question, we found it was necessary to take three strips at least from the internal surface of the uterus, generally starting from the fundus, coming down through the anterior wall, lateral wall and posterior wall. We found that there was more glycogen in the fundal portion than in the lower portion of the uterus, so that the picture evidently changes somewhat from the fundus to the internal os. We used an ordinary biopsy curette without the suction, for with the suction we found that we lost some material.

Many sections have to be restained. There is a new technique, but we still use carmine, for it gives a more satisfactory result than the old glycogen stain.

PELVIC LYMPHADENECTOMY IN THE TREATMENT OF CERVICAL CANCER*

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METASTASES in the regional pelvic lymph nodes have long constituted a stumbling block in the treatment of cervical cancer. In many instances, glandular involvement occurs only in association with extensive local growth, making a combination which spells doom for the patient. In other instances, regional node metastases exist even when the local growth is early enough to permit surgical eradication or destruction by radiation. It is in the latter group of cases that we are interested, for in them there exists at least the possibility of removing or destroying all the involved tissues. Forty odd years ago, the attempts to meet the problem were surgical; the regional glands were excised in the course of operations to remove the entire uterus, cervix, parametria, and upper vagina. The applicability of the surgical method was, however, limited by the operability of the local growth and by the high mortality entailed by such extensive procedures. It should be appreciated, of course, that operation was the *only* method of treatment available at that time, and that therefore as many cases as possible were subjected to the procedure. "Inoperable" meant actually impossible to remove. A high mortality naturally resulted from attempts to remove rather far advanced growths. As high voltage roentgen therapy reached an effective stage of development 15 years ago, the possibility of destroying cancer in the parametria and in the regional glands by this means moved to the fore. However, there still remained a group of cases in which the local cervical response to radiation promised much, yet death occurred soon after presumably because of the survival of cancer in the regional nodes. It appeared that metastatic cancer in lymph nodes was much more insensitive to radiation than the parent tumor, at least, it should be added, to the radiation available at that time. These considerations led the late Dr. Frederick Taussig to suggest a surgical resection of the regional pelvic lymph nodes as a supplement to radiation in the early inoperable group of cases.

His first operation was performed in October, 1930, and his last report, published in the Fall of 1943, gave the details of 175 such operations. Independently, at about the same time, Leveuf, in France, had a similar idea, and since then a small number of such operations

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(Leveuf, Michel-Bechet) have been performed in that country. In 1936, Duncan reported three cases of lymphadenectomy and suggested the use of interstitial radon seeds and ligation of the uterine arteries as adjunct to the procedure. In 1935, being impressed by Taussig's reasoning, we at the University of California Hospital, started to perform this operation upon certain selected patients. A small series of cases has since been accumulated, upon which are based the results and impressions contained in this paper.

TABLE I. INCIDENCE OF GLANDULAR INVOLVEMENT
(FROM THE LITERATURE)

AUTOPSY CASES	PER CENT	OPERATIVE CASES	PER CENT
Wagner	50	Kundrat (80 cases—serial sections)	32.5
Williams	72	Brunet (47 cases—serial sections)	51
Dittrich	40	Kermauner (73 cases—serial sections)	43.8
Blau	33	Sampson (19 cases—serial sections)	47
Schauta (50 cases, serial sections)	64	Bonney (500 cases)	40
Warren (1933)	63.7	Taussig (175 Stage II cases)	26.8
Behney (1933)		Baisch (52 cases—parametrium clinically free)	19.2
(Any metastatic lesion)		Leveuf and Godard (36 cases status unknown)	50
80 treated patients	21.2	Leidenius (21 cases—Wertheim)	28.6
86 untreated patients	44		
Morton (1935) (36 cases)	44.4		
Pearson (1936) (57 cases)	59		

SERIAL SECTION STUDIES			
PARAMETRIUM INVOLVED		PARAMETRIUM FREE	
Schauta	Approximately 50 per cent	Schauta (10 cases)	20.0
Brunet		Oehlecker (35 cases—collected, Schauta 10, Oehlecker 7, Baisch 18)	31.0
Baisch		Kundrat (36 cases)	11.1
Kermauner		Sampson (10 cases)	30.0
Kundrat			
Sampson			

The Incidence of Gland Involvement

Of great importance in deciding the indications for such a procedure as lymphadenectomy is a knowledge of the incidence of glandular involvement, particularly in relation to the degree of advancement of the local growth. Unfortunately the literature does not contain a really satisfactory study of the incidence of glandular involvement. Most of the available figures were obtained shortly after the turn of the century and were derived from two main sources; from autopsy cases, and from cases in which the radical operation had been performed. In the autopsy cases the disease was advanced and terminal, and in many instances the results were unconfirmed microscopically. They *do* afford us, however, an inkling of the peak figures. More recent autopsy studies, several of which are included in Table I are of less value, since in most instances varying amounts of radiation had been employed before death, and this may have altered the picture. The figures based upon operative cases are of limited significance because there is no way of knowing just how completely the glands were removed, nor is it possible to know the finer shadings in the stages of advancement of the disease at the time of the operations. This is

readily understood when one recalls that in those days all cervical cancers were lumped into three great groups—operable, borderline, and inoperable. Even so-called operability has varied widely as the following figures testify:

Franz	81 %
Bonney	63 %
Wertheim	46 %
Stoeckel	70 %
Brunn	68 %
Zweifel	58 %
Ward	25.9%
Regaud	18.3%
Healy	24.5%
Lynch	30 %

These variations must have been due largely to individual differences in the interpretation of operability. Bonney estimated that he had operated upon 63 per cent of the patients presenting themselves to him for treatment. At the University of California, we have operated upon only 10 per cent of our cervical cancer cases although we have considered 30 per cent of the cases operable so far as the local extent of the growth was concerned. Obviously, Bonney has regarded as operable, many cases which we would have deemed too advanced for surgery. This wide variation in the clinical stage of advancement in cases operated upon, limits seriously the value of the figures quoted insofar as they pertain to a correlation with the extent of the local growth.

There have, however, been a few investigations in which attention has been focused more sharply on this point. Serial section studies of the tissues obtained at radical operations have been reported by Schauta, Baisch, Brunet, Oehlecker, Kundrat, Kermauner, and Sampson. All of these observers found an incidence of approximately 50 per cent glandular involvement in cases in which parametrial invasion was confirmed by microscopic examination. In cases in which the parametrium was microscopically free of cancer, Schauta found the glands involved in 2 cases out of 10; Oehlecker, in 31 per cent of 35 collected cases (Oehlecker 7, Schauta 10, Baisch 18); Kundrat, in 4 cases out of 36; and Sampson, in 3 out of 10 cases. In interpreting these figures, one should bear in mind that parametrial involvement or its absence as determined by the microscopic examination of serial sections does not always correspond with the palpatory findings on pelvic examination. The parametrium may be clinically free, yet actually contain cancer, or it may be indurated (by inflammatory reaction) yet contain no cancer. Since the determination of operability is inevitably linked with the palpatory findings, it becomes even more difficult to interpret the figures quoted. Other reliable findings which are less pertinent, but nevertheless interesting in this connection are as follows: Kundrat found involved glands in 32.5 per cent of 80

operative cases (serial sections); Kermauner, 43.8 per cent in 73 cases (serial sections); Brunet, 51 per cent in 47 cases (serial sections); Sampson, 47 per cent in 19 cases (serial sections); and Bonney, 40 per cent in 500 cases (*no* serial sections). Additional figures are given in Table I. One can conclude that parametrial involvement connotes glandular involvement in about one-half the cases, and uninvolved parametria indicate glandular metastases in one-third or less of the cases. Closer correlations cannot be derived from the literature.

The older studies have elucidated several interesting points, however. Winter, Baisch, Leveuf, Taussig, and others have shown that the so-called first stage glands comprising the obturator, hypogastric, ureteral, and sacral groups, were almost always involved first, while the second stage glands, such as the inguinal and lumbar groups, were involved usually only late in the disease, and, with the exception of 5 to 10 per cent of these cases, only after involvement of the first stage groups. These facts are of practical significance in that an attack upon the first stage glands, either operative or by radiation, might logically prove valuable, except late in the disease, or where there is palpable evidence of involvement of the second stage glands.

It has also been shown by many that gross enlargement of glands did not necessarily mean metastatic involvement. Conversely, unenlarged glands have been found involved by cancer. Finally, it has been observed that glandular metastases sometimes occurred even when the local cervical growth still remained clinically confined to the cervix, although the glands occasionally remained free even after considerable parametrial spread, a fact which must account for the cures which were obtained by surgery in cases with a rather extensive growth.

Selection of Cases

Taussig chose for his operations not the very early cases, because of the rather insignificant incidence of glandular involvement, nor the advanced cases, because of the improbability of curing the local growth, but the borderline cases (Stage II, *League of Nations Classification*). In this group, he felt that the chance of curing the local growth by radiation was relatively good, yet the rather high incidence of glandular spread often resulted in recurrence. In some cases he performed the operation before roentgen therapy and in others, immediately afterward. Our choice of cases has differed slightly in that we have selected for operation only those in which the immediate local reaction to radiation has been good, whereas, Taussig has performed his operations more routinely, and before he has had an opportunity to observe the character of the local reaction. Our feeling has been that it was useless to resect the regional glands if there was not a reasonable chance of a successful outcome so far as the cervix proper was

concerned. At that, we have often been mistaken, as death has not infrequently followed because of local recurrence. Our material is set forth in Table II.

TABLE II. PELVIC LYMPHADENECTOMY—65 CASES

	CASES WITH GLANDS INVOLVED	CASES WITH GLANDS FREE	TOTAL
A. Simple lymphadenectomy the object (Stage III Schmitz cases)			
Lymphadenectomy alone	6	19	25
Lymphadenectomy plus incidental hysterectomy	2	6	8
Failed*	2	0	2
Inspection only†	0	2	2
Totals for group	10	27	37
B. Hysterectomy the object but lymphadenectomy only performed			
Stage I	1	0	1
Stage II	1	3	4
Totals for group	2	3	5
C. Wertheim hysterectomy plus lymphadenectomy			
Stage I	0	5	5
Stage II	2	14	16
Stage V	1	1	2
Totals for group	3	20	23
Grand Totals (A, B, and C)	15	50	65

*In two, the glands were so extensively involved that removal was impossible. In one, cancer was later proved at autopsy. In the other, the patient died of obvious carcinomatosis though autopsy was not permitted.

†Twice the operation was discontinued after palpation revealed no enlarged glands. In all other cases the gland-bearing tissues were removed whether glands were palpable or not.

At the University of California, the Schmitz classification has been used so that it is not possible to make direct comparisons between our material and that of Taussig. As well as performing gland resections per se in our Stage III Schmitz cases in which the local cervical reaction to radiation was good, we have taken pains to resect the glands in earlier cases in which the Wertheim operation was being carried out. In a few instances when we have entered the abdomen for the express purpose of removing the glands having found the cervical region freely movable, we have performed the radical operation in addition. The average age of the 61 patients in whom the operations were completed was 41.8 years. The majority of the women were young as may be seen in the accompanying tabulation:

26 to 30 years	5 cases
31 to 35 years	10 cases
36 to 40 years	11 cases
41 to 45 years	17 cases
46 to 50 years	6 cases
51 to 55 years	6 cases
56 to 60 years	6 cases

In 35 cases, the patients received courses of high voltage x-radiation in addition to approximately 4,500 mg.hr. of radium distributed in and about the cervix before operation. The dose of roentgen therapy

varied between 2,000 and 4,000 r. to each of 4 fields, 2 anterior and 2 posterior. Both 1,000 kv. and 200 kv. machines were used. In 28 instances, radium only was used in small doses as preparation for the radical operation.



A.



B.

Fig. 1.—Degenerate cancer cells in regional lymph nodes. A, after vaginal radium only; B, after radium and x-radiation.

The operation which we have employed has been patterned after that developed by Taussig. It involves a laparotomy approach, the exposure of the depths of the broad ligaments and the lateral walls of the pelvis after removal of the tubes and ovaries, and resection of the gland bearing areolar tissues lying in the bifurcations of the common iliac arteries and in the obturator fossae. The areolar tissue about the uterine arteries and the ureters, as well as that lying about the iliac veins just before their exit beneath Poupert's ligaments have also been removed when glands could be palpated in these structures. The operations have not been difficult though occasionally they have been complicated by troublesome hemorrhage from the plexus of uterine veins. In two cases in which the Wertheim operation was performed in addition to lymphadenectomy, death from cellulitis and generalized pelvic infection followed within a period of two months; no cancer remained at autopsy. There has been no mortality from the operation of simple lymphadenectomy alone. In one case a broad ligament hematoma became infected and resulted in a prolonged illness from which the patient finally recovered. Obesity and old age have been considered contraindications.

Pathological Findings

If we omit the two cases in which the gland bearing tissues were palpated but not removed, lymph node metastases were found in 15 of the 63 cases. The figures relating to the incidence of glandular involvement (Table III) mean very little as such because of the small number and the heterogeneity of the cases, and because of the varying amounts of radiation employed. In many cases there were no grossly enlarged glands, yet invariably one or two and sometimes more glands were discovered in the areolar tissues from each of the hypogastric and obturator areas; these tissues were subjected to careful scrutiny in the laboratory. With two exceptions, the involved glands (15 cases) were grossly enlarged. There were many instances of enlarged glands which did not contain metastases. Several sections were cut from each recognizable gland, but no attempt was made to prepare serial sections. This is an obvious drawback to the study, and it must be admitted that serial sections might have revealed additional metastases. In the 13 cases in which metastases were found microscopically in glands, there was no question of their existence. These deposits

TABLE III. INCIDENCE OF GLANDULAR INVOLVEMENT

	CASES	CASES WITH GLANDS INVOLVED	PER CENT
Stage I	6	1	----
Stage II	20	3	15.0
Stage III	35	10	28.6
Stage V	2	1	----
Total	63*	15	23.8

*Omitting the 2 "Inspection only" cases.

were all squamous cell and all were similar to their parent tumors. In two cases (Fig. 1) some degree of degeneration appeared to be present. In one of these, the patient had received radium therapy preoperatively but no x-radiation (A), and in the other the patient had received 3,735 r. to left anterior and posterior fields (1,000 kv.) and 2,300 r. to right anterior and posterior fields (200 kv.), yet had this metastasis in the left obturator gland (B). In 11 cases there was no degeneration of consequence. (In only one of these 11 had the patient received roentgen therapy preoperatively.)

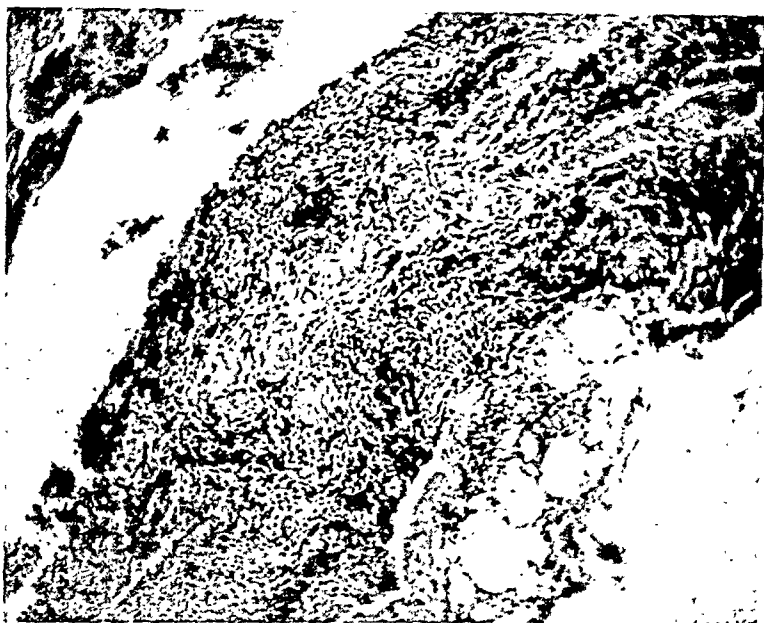


Fig. 2.—Fibrosis and hyalinization in a regional lymph node. This picture was observed both with and without preoperative x-radiation.

In other respects, it was difficult to distinguish the radiated (x-ray) from the nonradiated glands. In all instances, there were varying degrees of endothelial and follicular hyperplasia. Fibrosis and hyalinization were common but were not distinctive, having been observed in 24 of the 33 cases in which preoperative x-radiation had been employed, but also in 10 of the 28 cases in which the patients had received no roentgen therapy. (Fig. 2.) No correlation with the amount of x-radiation could be established. A point of interest was the finding of glandular inclusions in the glands from two cases. These we interpreted as benign. Such a finding has been the bone of much contention in France. Schauta, Brunet, Gricouroff, and others have reported similar findings and interpreted these structures as endometrial glands. Wertheim found lymph nodes containing glandular inclusions 48 times in 500 operative cases. Basing his belief upon the subsequent course of these patients, he regarded such inclusions as benign. Michel-Bechet and Taussig have made similar observations. These authors favor the idea that the condition is one of endometriosis.

Of great interest are the figures on the incidence of glandular involvement when the cases are broken down into those in which the patients received preoperative deep x-ray therapy, and those in which they did not. (Table IV.) Obviously, the figures are too small to regard as true reflections of the percentages of glandular involvement to be expected in patients treated with and without radiation. However, the 39.3 per cent glandular involvement following *no* preopera-

TABLE IV. INCIDENCE OF GLANDULAR INVOLVEMENT IN RELATION TO PREVIOUS ROENTGEN THERAPY

	STAGE	CASES	GLANDS NORMAL	GLANDS INVOLVED	PER CENT
No preoperative roentgen therapy	I	6	5	1	
	II	16	12	4	
	III	5	0	5	
	V	1	0	1	
	Total	28	17	11	39.3
Preoperative roentgen therapy	II	4	4	0	
	III	30	26	4*	
	V	1	1	0	
	Total	35	31	4	11.4

*Includes the 2 cases in which involvement of the glands was so extensive that removal was impossible.

tive x-radiation would seem to be quite significant when compared with the 11.4 per cent glandular involvement in cases in which roentgen radiation was used, particularly when we consider that the latter group contained many more advanced cases than the former. If this highly suggestive difference in the incidence of glandular involvement in the two groups of cases can be substantiated by future experience, one would like to interpret it as evidence that high-voltage roentgen therapy is capable of destroying, and often does destroy cancer in the regional nodes. In Taussig's last report, the incidence of glandular metastasis was given as 26.8 per cent which was lower than that shown in previous reports (33 per cent in 1936). He remarked, "Apparently, this was due to the prolonged and heavy x-radiation patients have received preoperatively in recent years." However, he believed that cancer metastases might frequently be rendered unrecognizable (by radiation) but not wholly destroyed, and thus that the operative removal was still justifiable.

Results

The actual five-year results in this group of cases are of little significance in evaluating this procedure as a method of treatment. (Table V.) It is of interest that the lives of at least three women from whom glands involved by cancer were removed, were apparently saved by the procedure. Of the 10 patients in the five-year group in whom the glands were involved, only three survived, while of 18 patients in whom glandular involvement was not found, 16 survived the five-year period. While these figures seem to point a very ominous finger at

TABLE V. RESULTS

Total five-year cases	28
<i>Alive and well after five years</i>	19
Number in which involved glands were found	3
Number in which no involved glands were found	16
<i>Died in less than five years</i>	9
Number in which involved glands were found	7
Number in which no involved glands were found	2

glandular involvement, at least 5 of the 9 deaths were due to the local cervical recurrence and invasion of cancer, and not to the existence of cancer in the glands.

Discussion

If the premise upon which Taussig based his operation, namely, that metastases in lymph nodes are peculiarly resistant to radiation, can be substantiated, then his procedure deserves a much more extended trial. If however, it can be shown that modern x-radiation may actually destroy metastatic cancer in lymph nodes, then this nonoperative and possibly more comprehensive method may prove superior. The number of cases so far subjected to the procedure of lymphadenectomy is insufficient to determine definitely its sphere of usefulness in the treatment of cervical cancer. The distinctly lower incidence of glandular involvement in our series when the operation was carried out after x-radiation suggests that modern roentgen techniques may make lymphadenectomy unnecessary. Certainly the results call for an extension of experience in cases subjected to preoperative x-radiation as compared with those in which no preoperative x-radiation has been employed as this appears to be the crux of the whole matter.

References

1. Baisch, K.: Arch. f. Gynäk. 75: 273, 1905.
2. Behney, C. A.: AM. J. OBST. & GYNEC. 26: 608, 1933.
3. Bonney, V.: J. Obst. & Gynec. Brit. Emp. 48: 421, 1941.
4. Brunet, G.: Ztschr. f. Geburtsh. u. Gynäk. 56: 82, 1905.
5. Ducuing, Guilhem, and Dieulafe, R.: Bull. Soc. gynéc. et d'obst. 27: 724, 1938.
6. Frank, R.: Gynecological and Obstetrical Pathology, New York, 1922, D. Appleton-Century Co.
7. Gricouroff, G.: Mém. Acad. de chir. 62: 1384, 1936. Bull. Assoc. franç. p. l'étude du cancer 25: 759, 1936.
8. Kermauner, F.: Halban-Seitz, Pathol. u. Biol. d. Weibes 4: 843, 1928.
9. Kundrat, R.: Arch. f. Gynäk. 69: 355, 1903.
10. Leidenius, L.: Acta obst. et gynec. Scandinav. 10: 32, 1930.
11. Leveuf, J., and Godard, H.: J. de chir. 43: 177, 1934.
12. Lynch, F. W.: Pelvic Neoplasms, New York, 1922, D. Appleton-Century Co., p. 221.
13. Michel-Bechet, R.: Mém. Acad. de chir. 62: 926, 1936.
14. Morton, D. G.: California & West. Med. 42: 345, 1935.
15. Oehlecker: Drusen untersuchungen bei 7 Fällen von Uteruscarcinoma, Berlin, 1903, O. Francke.
16. Sampson, J. A.: Am. J. Obst. 54: 433, 1906.
17. Schauta, F.: Monatschr. f. Geburtsh. u. Gynäk. 19: Part 4, 1904.
18. Taussig, F. J.: AM. J. OBST. & GYNEC. 28: 650, 1934.
19. Taussig, F. J.: AM. J. OBST. & GYNEC. 32: 777, 1936.

20. Taussig, F. J.: AM. J. OBST. & GYNEC. 36: 819, 1938.
21. Taussig, F. J.: AM. J. OBST. & GYNEC. 45: 733, 1943.
22. Taussig, F. J.: AM. J. ROENTGENOL. 41: 242, 1939.
23. Taussig, F. J.: AM. J. ROENTGENOL. 43: 539, 1940.
24. Taussig, F. J.: AM. J. ROENTGENOL. 45: 813, 1941.
25. Wagner: Der Gebärmutter Krebs eine pathologisch-anatomisch Monographie 6: 169, 2 Tafeln, Leipzig, 1868.
26. Warren, S.: Surg., Gynec. & Obst. 56: 742, 1933.
27. Williams, R.: Brit. Gynec. Fourn. 11: 529, 1895.
28. Winter, G.: Ztschr. f. Geburtsh. 27: 101, 1893.

Discussion

DR. WILLIAM P. HEALY, NEW YORK CITY.—During the past 25 or 30 years, radiation therapy has largely supplanted surgical procedures as the method of choice in the treatment of cancer of the cervix.

About 1930, Taussig was impressed by the large number of Group II (*League of Nations Classification*) cases of cancer of the cervix in which the primary disease was cured by radiation therapy, but the patients died of metastatic cancer. He assumed these deaths were largely due to the failure of the methods of radiation therapy then available to cure the cancer which already had involved the pelvic lymph nodes. It was in this relatively favorable group that it seemed to him possible to obtain more five-year cures by combining iliac or pelvic lymphadenectomy with radiation therapy.

In 1943, Taussig reported 175 lymphadenectomy operations done by him and his associates and he stated that the low primary mortality, about 1.5 per cent, and the relatively high survival rate in their five-year cases convinced him that this combination of surgery with thorough radiation in Group II cases of cancer of the cervix was of definite value. Many of us were favorably impressed by Taussig's views, but failed to follow the procedure except sporadically.

Dr. Morton's paper in which he reports 65 cases of pelvic lymphadenectomy is a valuable contribution to the subject. I am inclined to believe from his report that roentgen therapy was much more adequately administered in his cases than in Taussig's. This, of course, would be accounted for by improved technique and higher voltages in recent years. One must be impressed by the distinctly lower incidence of pelvic lymph node involvement in Morton's series when adequate roentgen radiation had preceded the operation. As he says, it would suggest that improvement in modern x-ray technique may make the operation of lymphadenectomy unnecessary.

In 1942, Healy and Twombly reported a study of 920 cases of primary cancer of the cervix treated at Memorial Hospital from 1932 to 1937. These cases were studied from the viewpoint of "The Effect on the Rate of Cure of Increased Roentgen Radiation to the Parametria." It was found that the more modern divided dose technique of roentgen therapy which requires about three weeks of daily treatments to accomplish definitely raised the five-year cure rate in all cases. Nevertheless, the best five-year cure rate that we were able to show in our Stage II cases was 50 per cent. Therefore, it would seem to me desirable, in fact an obligation, for us to add pelvic lymphadenectomy or some other surgical procedure to the combined radium and roentgen therapy in a selected list of our Group II cases of cancer of the cervix.

It seems to me that gynecologists are about to enter on a new era in the treatment of cancer of the cervix which has become feasible because of improved methods of anesthesia, better preparation for operation and better postoperative care because of the use of intravenous fluids, blood serum and whole blood, and lastly in the protective use of sulfa drugs and penicillin. It is my impression that we will henceforth carry out more extensive surgical procedures combined with radiation

therapy than has been done in the past 25 years, in properly chosen cases. I think the surgeon who fails to qualify for this will miss an opportunity, for in the final analysis surgery has always been the best approach to the treatment of cancer, and radiation, while useful and curative in certain cases, is not the final answer.

DR. LEWIS C. SCHEFFEY, PHILADELPHIA, PA.—Dr. Morton believes his operation indicated in those patients in whom regional node metastasis may exist through the primary cervical growth seems to have responded sufficiently well to irradiation. He recognizes, however, that while an apparently early lesion may already have spread to the regional nodes, one more advanced in appearance may be relatively localized, even with parametrial involvement.

I am particularly impressed with the high incidence of younger women in the series presented, 43 per cent, and wonder as a matter of interest how this selected figure compares with the general incidence of cervical carcinoma in women 40 years of age or younger in the University of California Clinic. At Jefferson Medical College Hospital 27 per cent of the cervix cancers occurred in women before the menopause.

All in all, Dr. Morton found lymph node involvement in 15 or 23 per cent of the 65 cases observed, but he is careful to state that one cannot exclude the possible effect of preoperative irradiation upon this finding. Of more importance, I think, is the breakdown of this figure which shows a decided advantage in favor of thoroughly employed preliminary irradiation therapy. These observations seem to demonstrate the potent effect of adequate irradiation on the regional nodes not only when the possibility of subsequent surgery is entertained, but in all advanced cases as well. That degeneration did occur in some of the lymph nodes is surely significant. Naturally, these findings must be substantiated by further work if we are to decide to rely solely upon irradiation therapy, or if we are to complement it by pelvic lymphadenectomy, or in some cases by radical hysterectomy.

Surgery has played no part in the treatment of cervical carcinoma in the Jefferson Clinic since 1923, two years after its establishment. The Group 1 and 2 patients (Schmitz classification) that we have encountered have amounted to but 12 per cent among nearly 500 patients seen, and that is one reason why we have depended upon irradiation therapy in practically all cases. Another reason has been the relatively satisfactory results seen with this therapy to date. Our most recently reported statistics show a five-year survival rate of 75 per cent in Group 1 patients, and 43 per cent in Group 2 patients, or a combined rate of 47 per cent in the so-called "early" cases. In view of what Dr. Morton has shown us today, together with the results of Dr. Taussig's earlier efforts, I shall feel derelict if we do not attempt work of a similar nature, even in Group 3 patients who have responded well locally to irradiation therapy.

DR. JOE V. MEIGS, BOSTON, MASS.—I have been immensely impressed by the work of Dr. Taussig, whose operating I observed in 1940. Dr. Lynch in California was very much interested at that time as to whether we should carry out Dr. Taussig's ideas or do radical hysterectomies.

I am now doing the Wertheim operation on those patients who are good surgical risks. We had felt before beginning work with this procedure that our mortality would be excessive. We have, however, now done about 65 Wertheim operations, that is, removing all the pelvic lymph nodes and taking out as much parametrium and as much vagina as possible, and there has been no mortality. Our low mortality is due to modern surgery and modern methods of taking care of the patient both before and after operation.

My objection to the Taussig operation is that the lymph node area about the cervix is not properly taken care of. Unless one removes this area, one cannot get all of the lymph nodes, although Dr. Taussig with whom I discussed this matter felt that radiation handles that particular area. We have found that 15 per cent of

our cases had positive lymph nodes. Cancer in a radiated cervix may recur after ten years and radium cannot destroy cancer in lymph nodes. It is my distinct impression that the Taussig operation is not sufficient and that it must have added to it the removal of the uterus and the parametrium. It is a formidable procedure, but in our hands at the present time, it is so successful that we feel we have a right to proceed further.

DR. MORTON (closing).—The average age of the patients operated upon is considerably less than that for our series in general. We selected the younger women for this operation because we felt that many of the older ones were not good operative risks.

Our usual routine is to give x-ray therapy first and the radium treatment later, particularly when the growth is bulky. The idea behind this routine is that a good deal of shrinkage and a good deal of cleaning up of the infection will result so that the radium can be applied more safely and effectively at a later time. However, we have reversed this order in certain cases, more particularly in those in which the growth was earlier or small in area. We have also reversed the order in older women where we felt we might not be able to carry through the x-ray therapy because of its drastic general effects. We feel that our results have justified the initial use of radium and the frequent omission of x-ray therapy in these types of cases. I am very much interested that Dr. Meigs has taken up the complete operation, and his reactions to it. As most of you know, Dr. Lynch, from whose service this series of cases was taken, has been much interested in the radical operation for a great many years, and yet the operation has been performed on not more than one-tenth of all the patients seen on his service. This seems to point to a very limited, though definite field of usefulness. While 30 per cent of our cases have been considered operable from the point of view of the local extent of the growth, in two-thirds of this operable group the radical operation was considered to be contraindicated by virtue of old age, obesity, or the like.

PREGNANCY AND OTOSCLEROSIS*

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(From the Department of Obstetrics and Gynecology, University of Illinois)

OTOSCLEROSIS is a chronic, nonsuppurative disease of the bony capsule of the ear surrounding the labyrinth which interferes with the function of hearing. This disease is characterized by progressive absorption of the normal capsular bone and replacement with new spongy bone. This bony change often leads eventually to stapedio-vestibular fixation and complete deafness. The site of predilection is above and in front of the oval window.¹ (Fig. 1.)

Otosclerosis or, as the French call it, otospongiosis, is found predominately in females, 66 to 79 per cent. Shambaugh² has estimated that 45 per cent of adult deafness is due to this disease. Fowler³ has suggested, and subsequent observations have substantiated his thesis, that routine histological examination of temporal bones will often reveal an existing focus which does not involve the footplate, and therefore, does not produce deafness. These facts then would suggest that otosclerosis is rather a common disease. Nash,⁴ on the other hand, states that no diagnosis of otosclerosis can scientifically be made without progressive deafness, Bezold's triangle, and a normal middle ear and eustachian tube. This author was able to make a definite diagnosis of otosclerosis in less than 6 per cent of 1,000 cases of deafness which he studied.

Politzer (over 50 years ago) first described otosclerosis, and since that time, it has been the subject of intensive study. Little knowledge, however, has been added during this period concerning its etiology. Early in these investigations the great importance of heredity was recognized and numerous families have been followed carefully. An interesting study covering 5 generations is reported by Ulrich⁵ as follows:

In the first half of the eighteenth century, a married couple in Zurich with perfectly normal hearing had 3 daughters congenitally deaf. Marriage of one daughter to a young man of normal hearing was forbidden but later consummated. This pair had several normal children but also 3 daughters congenitally deaf. Thus in 2 successive generations 6 deaf children were born, with only one deaf parent. Actually all had originated from a pair of normal-hearing persons. Three hundred and ninety decendants of this family were traced, but no further cases of deafness could be ascertained.

The first study of otosclerosis in identical twins was reported by Albrecht⁶ in 1932. Since this time several additional cases have been

*Read at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

observed by Rodin⁷ in 1933, Shambaugh and Shambaugh, Jr.,⁸ in 1933, and Shambaugh,⁹ Jr., in 1935. In 1941, Hagens¹⁰ recorded the family history of a set of identical twins with their audiometric tracings. The mother of these twins came from a family of 10 children, 8 of whom were deaf. An increase in deafness occurred in the mother shortly after the birth of the twins. A similar decrease in sound perception occurred in one of the twins after the birth of her baby. These changes, however, are not substantiated by audiometer readings. The hearing defect in the second twin was not severe enough to cause her to seek medical aid. On examination however, it was found to be bilateral, and tests permitted a diagnosis of otosclerosis. More recently Fowler¹¹ records the case histories of 3 sets of deaf identical twin girls. In only one of these was there any impressive familial history of deafness, a grandmother and a maternal aunt. The mother herself had perfect hearing. No effect of menstruation or childbearing on hearing could be determined in these twins except one girl had more difficulty in hearing when she was nervous at menstruation.



Fig. 1.—Showing area of otosclerosis. A, in region of oval window; B, stapes.

Guggenheim¹² in his monograph concludes that otosclerosis is primarily an hereditary disease. In this splendid work the author reports a careful study of a 6-week-old, perfectly preserved fetus from a classic case of otosclerosis. Rather typical histologic findings were present in the capsular bone of the ear. He makes a plea to those of us

engaged in obstetrics for help in the further collection of similar valuable material. Fetuses, in any stage of their development, born of mothers suffering from deafness which become available to any of us for post-mortem examination should be carefully studied by a competent otological pathologist. Our group could profitably join with the otologists in a study of this condition during pregnancy.

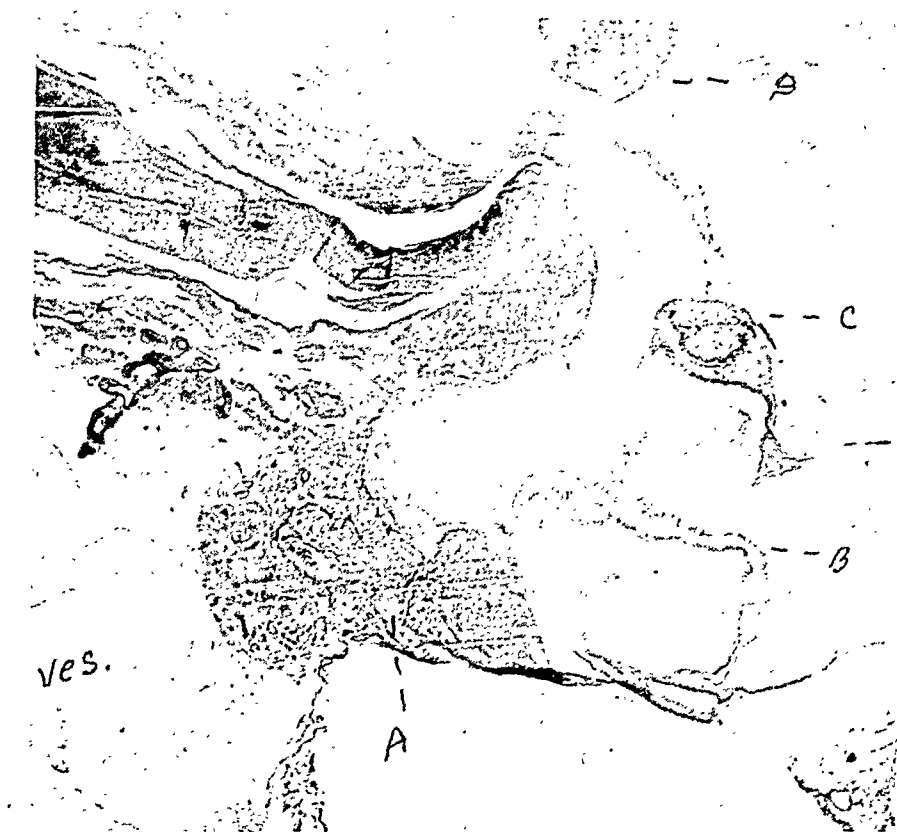


Fig. 2.—Showing area of otosclerosis. A, stapes; B, incus; C, malleus, D, vestibule (Ves).

Most American standard textbooks of obstetrics do not mention otosclerosis.¹³⁻¹⁵ or they list it among the indications for therapeutic abortion.^{16, 17} Adair and Steiglitz¹⁸ state that there is a familial tendency to otosclerosis in approximately 50 per cent of cases but that pregnancy is almost negligible as an etiological factor. Adair¹⁹ believes that deafness and tinnitus are increased in only about one-third of cases. He feels that the condition does not threaten life and is, therefore, not an indication for prevention or interruption of pregnancy. We can corroborate his statement that the desire for pregnancy will often outweigh the possibility of further impairment in hearing and is rarely an indication for the interruption of pregnancy. Personal observation of several cases of pregnancy complicated by this form of deafness plus the desire to advise adequately a sterility patient suffering from otosclerosis led us to this present study. The conclusions are based on the available literature, personal observation of 5 afflicted patients, and a

compilation of as many case records as we were able to collect from the many kind friends who have allowed us to use their records. (Total 72.)

A review of the literature suggests several important but confusing angles to the present concept of the importance of marriage, pregnancy, abortion, sterilization, castration or nursing on the transmission of otosclerosis. Widespread interest in these questions was first aroused by many reports occurring in the German literature, although the first laws dealing with the subject were enacted in a small liberal Swiss canton.⁵ Shambaugh,²⁰ following a review of the literature in 1938, says, "The German law for the prevention of the propagation of hereditary disease is responsible for the continued interest in hereditary deafness in the German literature." One is forcibly struck by the obvious effect of the idea for the betterment of the race on the therapeutic

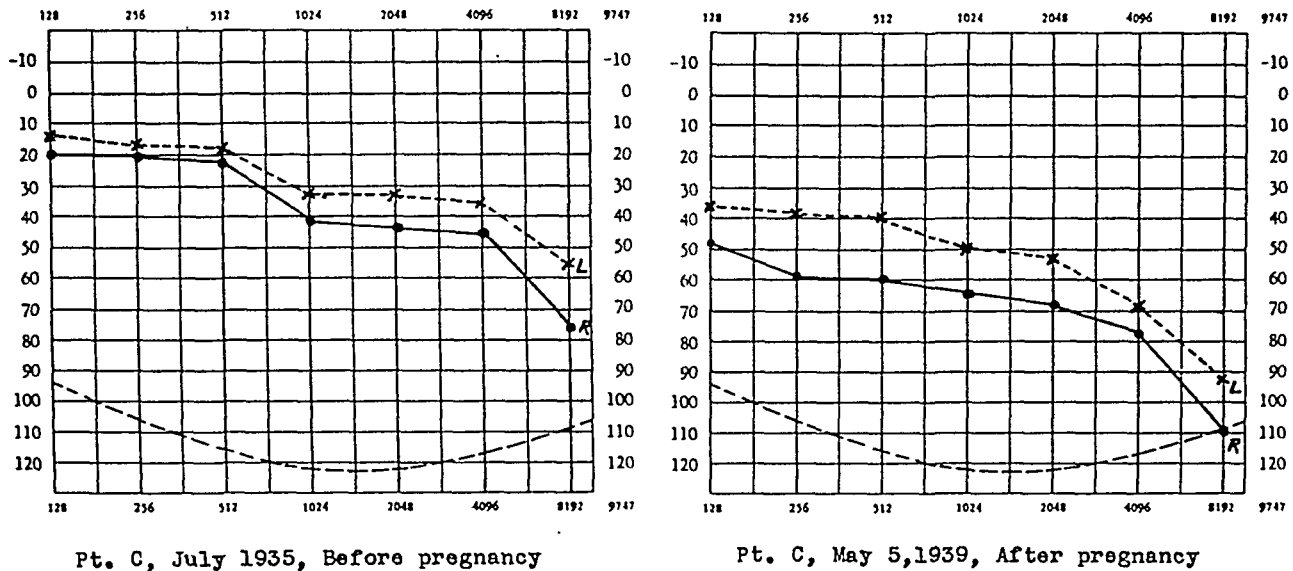
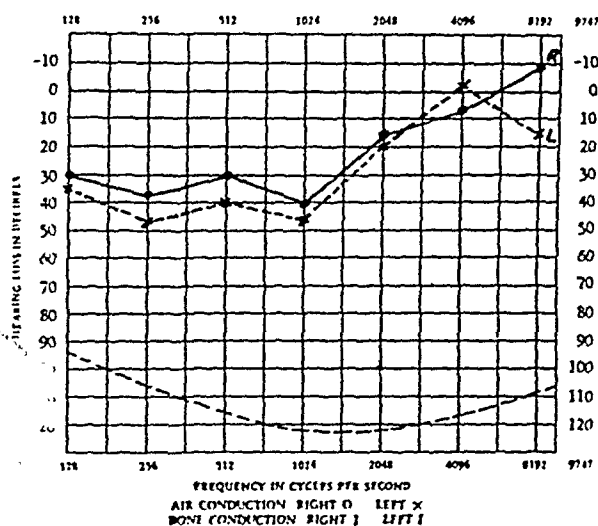


Fig. 3.

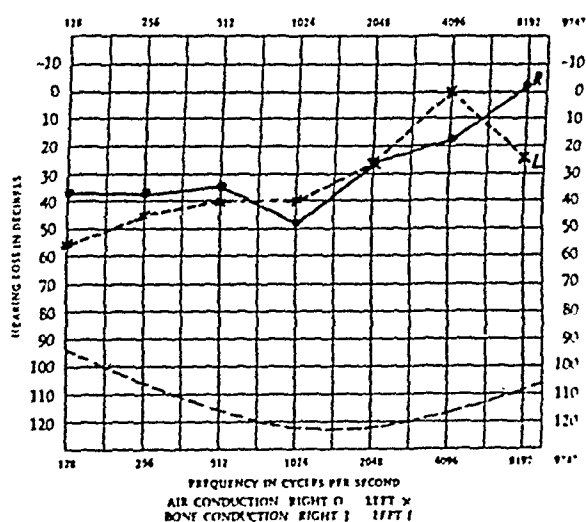
measures advised and the conclusions drawn by Teutonic authors. Analysis of a problem on the basis of political ideology does not lend itself to scientific accuracy. In a similar manner, religious precepts have apparently influenced many of the French otologists in arriving at conclusions directly opposed to those of their German confreres.²¹ As yet, no unbiased agency has had sufficient personal or collected experience to speak authoritatively on the subject.

While most authorities are agreed as to the great importance of heredity, many of them have suggested other possible etiological or contributory factors in otosclerosis. Fowler²² has expressed the belief that head colds and the development of the condition are related. Selfridge²³ suspected a faulty diet, especially one low in citrus fruits, milk and eggs. Many otosclerotics have poor crumbling teeth without much evidence of infection. The identical twins, previously mentioned, were both wearing upper plates at nineteen years of age.

Bunch²⁴ has observed a similar dental difficulty especially in those patients with low metabolic rates. Davenport²⁵ concludes that otosclerosis represents genetically two dominant factors, one sex linked. Symptoms of otosclerosis are usually manifested at puberty or later. An increase in the deafness often occurs at the time of the menopause.²⁶ Most authorities are agreed that the disease is at least temporarily adversely affected by pregnancy and lactation. However, Guggenheim says there is no scientifically proved glandular etiological factor in this disease. Fowler could find no abnormality of general metabolism in a large number of patients thus affected. Weber²⁷ is quite sure that the local form of osteodystrophia fibrosa is due to some local disturbance in metabolism. Despons has found that consanguineous marriages frequently result in this condition. Gottlieb²⁸ doubts the validity of genetic studies on the heredity of deafness and suggests persisting environmental factors leading to nutritional and toxic disorders as a possible cause.



Pt. B, July 24, 1936, Before pregnancy



Pt. B, September 30, 1937, 3 months after delivery.

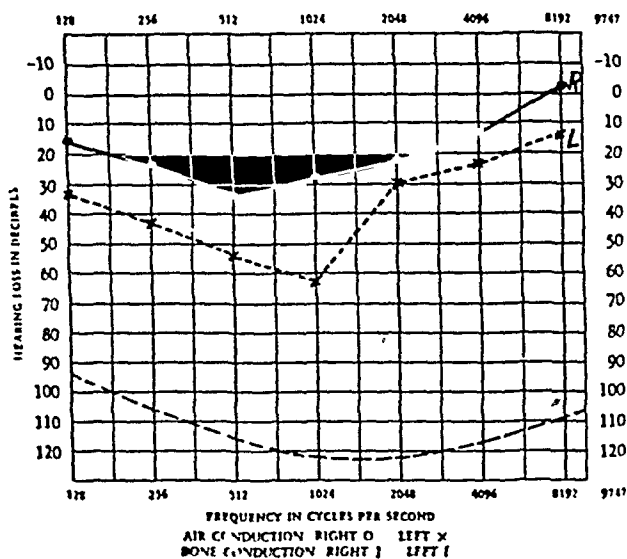
Fig. 4.

Falta,²⁹ in a study of 76 women in whom otosclerosis appeared after the fortieth year, noticed that 11 developed the difficulty with hearing during the climacterium. Furthermore, 8 of these 11 women had borne several children without any apparent impairment of hearing.

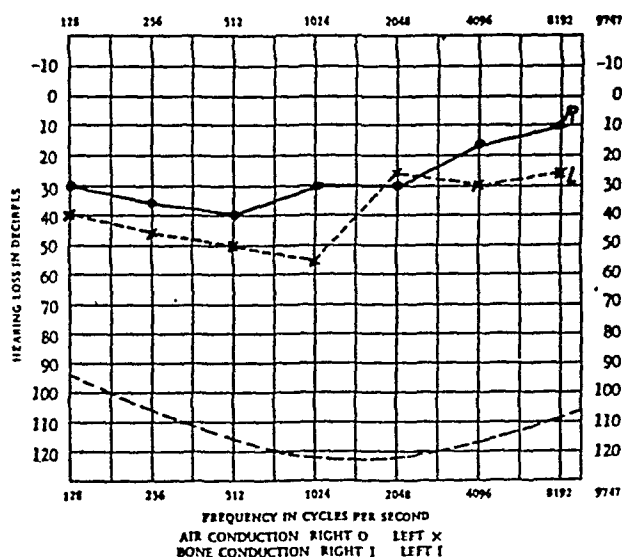
Despons says that total sterilization or an oophorectomy are sometimes held responsible for, or predispose to, the advance in deafness. Escat²¹ had a case in which hysterectomy was followed by deafness. Schmidt,²⁰ in a study of 106 cases of otosclerosis, says the deafness increased under various conditions, i.e., trauma, prolonged anxiety or excitement, menstruation, appendicitis and many other illnesses.

Despons in summarizing a symposium on the subject of otosclerosis and pregnancy says, "In a few years (otosclerosis) will probably be

listed among social evils and eugenics may require prophylaxis. Recently, the tendency has been to favor abortion in otosclerosis, not so evidently in France as across the Rhine." Despons goes on to quote Goerke. "Abortion is not indicated in pregnancy with otosclerosis if the deafness is minimal. If preceding pregnancies have increased it and there exist ear noises and psychic depression, removal of the ovaries or sterilization by x-rays should be advised to prevent further increases in deafness."³⁰



Pt. A, August 31, 1925, Before marriage



Pt. A, January 6, 1928, 4 months pregnant

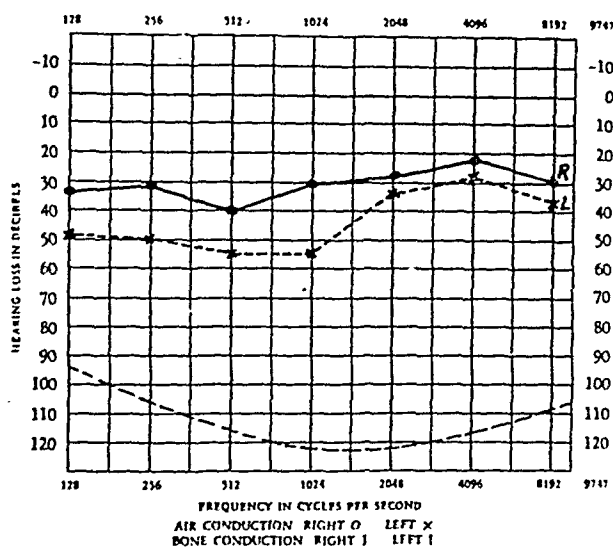
Fig. 5.

Mortimer and his co-workers³¹ have shown the marked changes which occur in the mucous membranes of the respiratory tract during pregnancy. These investigations have also produced a similar change of the respiratory passages in the *Macaca* monkey by the administration of estrogenic hormones. A definite perivascular edema in the submucosa and changes in the connective tissue occurred which are very similar to those found in the sex skin about the genitals.

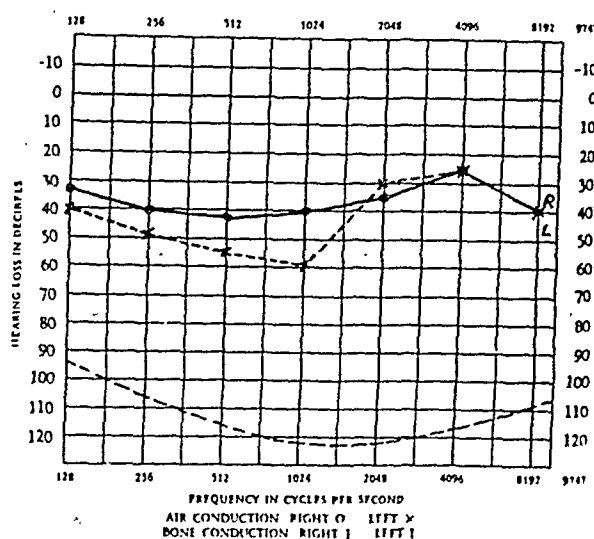
It seems reasonable to believe that the high estrin levels which occur during pregnancy in the human female may exert a similar effect on the mechanism of hearing. Otological complaints during pregnancy are very common, but most of them tend to disappear when involution has occurred. These facts may almost entirely account for the frequent appearance of otosclerosis for the first time during the primiparous pregnancy. In fact these changes may adequately explain a large proportion of the loss of hearing during the course of reproduction. Further clinical and experimental observations concerning the effect of pregnancy on the respiratory and auditory systems in the human female are essential for the further consideration of these problems.

Greifenstein,³² studying 98 women with otosclerosis in a group of 122 patients with difficulties in hearing who had been reported to the state

for therapeutic abortion and sterilization, attempted to explain the obvious variations in indications and results in the then current methods for the estimation of hearing. These difficulties arose because at that time there was no exact definition of what constituted "worse hearing."



Pt. A, August 28, 1928, 2 months after delivery



Pt. A, July 8, 1932, after second pregnancy

Fig. 6.

Now, with the audiometer, we have a more exact method of measuring loss or gain in hearing.³³ This can be measured in decibels and the differences of sound perception in various tonal areas can be determined. (Figs. 3-6.)

If the metabolic concept of the etiology and progress of otosclerosis is tenable, recent improvement in prenatal care may account for at least some of the less pronounced losses of hearing during pregnancy shown

TABLE I. STATISTICS

Cases with audiograms		
Personal communication	13	
From the literature	5	
Total		18
Cases without audiograms		
Personal communication	19	
From the literature	35	
Total		54
Number of patients in whom hearing remained the same or otologist felt decrease in hearing was that which might be expected during the normal progress of the disease		
Cases without audiograms	24	
Cases with audiograms	8	
Number of patients in whom hearing was decreased beyond normal expectancy		
Cases without audiograms	30	
Cases with audiograms	5	
Number of cases in which deafness first occurred during pregnancy	14	

TABLE II. CASES WITHOUT AUDIOGRAMS (BY PERSONAL COMMUNICATION)

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS	
M. R.	39	0	Para 1	Pregnancy did not influence hearing	Goldberger, M. A.
H. Z.	32	Deafness in family	Para 2	Pregnancies did not influence hearing	
P. K.	34	0	Para 2	Slight increase in deafness	
L. B.	-	0	Para 2	Slight deafness during second pregnancy	
W. M. C.	39	0	Para 4	Deafness appeared during second pregnancy. Improvement after delivery	Cody, C. C.
H. W.	41	0	Para 1	Pregnancy did not influence hearing	Dieckmann, W. J.
D. M.	28	0	Para 1	Pregnancy did not influence hearing	
A. B.	37	Mother, brother	Para 3	Pregnancy did not influence hearing	Johnston, R.
F. C. R.	35	0	Para 1	Pregnancy did not influence hearing	Galloway, C. E.
E. M. K.	41	0	Para 1	Pregnancy did not influence hearing	
R. G. B.	27	0	Para 1	Pregnancy did not influence hearing	
R. D.	46	0	Para 2	Deafness developed during first pregnancy	
J. S.	-	Paternal and maternal grandparents, father, brother	Para 3	Pregnancy did not influence hearing	Johnston, R.
T. C.	-	Mother, sister (twin)	Para 3	Deafness appeared during first pregnancy, increased during second and third	Gough, J.
R. H.	40	0	Para 2	Deafness increased after pregnancies	
E. M. A.	34	Father	Para 3	Deafness appeared during first pregnancy, increased after second and third	Shambaugh, G. E., Jr.
M. K.	47	0	Para 11	Deafness appeared during last 3 months of eighth pregnancy. Three subsequent pregnancies	Shambaugh, G. E., Jr.
D. F.	39	0	Para 2	Otosclerosis? Hearing tests showed nerve deafness. Deafness progressive, with increase after both pregnancies	Shambaugh, G. E., Jr.
B.	32	Paternal grandfather	Para 2	No appreciable change in hearing except natural progression indicated by biannual audiograms	Biehn, J. F.

TABLE III. CASES WITHOUT AUDIOGRAMS (FROM THE LITERATURE)

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS
21	30	0	Para 1, age 22	Deafness appeared during pregnancy
4	33	Father, sister	Para 1, age 27	Deafness appeared during pregnancy
6	66	0	Para ?	Pregnancy did not influence hearing
7	26	Maternal grandmother	Para ?	Deafness appeared during pregnancy
9	37	0	Para ?	Pregnancy did not influence hearing
12	52	Maternal grandfather	Para ?	Pregnancy did not influence hearing
14	31	Mother	Para 3	Hearing worse after pregnancies
15	28	Mother	Para 1	Deafness appeared after pregnancy
16	31	0	Para 2	Deafness appeared after second pregnancy
18	38	0	Para 2	Deafness increased after both pregnancies
20	26	Mother	Para 2	Deafness increased after both pregnancies
21	54	0	Para ?	Pregnancy did not influence hearing
22	41	0	Para 2	Pregnancy did not influence hearing
23	35	Father	Para 2	Pregnancy did not influence hearing
29	24	Uncle, aunt	Para 1	Pregnancy did not influence hearing
34	29	0	Para 4	Deafness increased after first pregnancy
35	38	0	Para 1	Deafness increased during pregnancy
36	33	Mother	Para 2	Pregnancy did not influence hearing
37	24	0	Para 2	Deafness increased after both pregnancies
4-B-42	?	Brother, sister	Para 3	Pregnancy did not influence hearing
1-C-4		Father, brother, grandfather, 2 uncles, cousin	Para 10	Deafness increased after pregnancies
1-2-C-1		Mother, 2 sisters, grandfather, 3 aunts	Para 4	Deafness increased after pregnancies
1-B-4		Father, 2 sisters	Para 9	Deafness increased after pregnancies
1-2-C-5		Mother, 2 sisters, grandfather, 3 aunts	Para 2	Deafness noticed after pregnancies
1-2-C-8		2 sisters, 2 uncles, aunt, grandaunt	Para 4	Deafness increased after pregnancies

¹Bunch, C. C.: Ann. Otol., Rhin. & Laryng. 43: 344, 1934.

²Schick, H. F.; Goldstein, M. A.: Laryngoscope 46: 731, 1936.

TABLE III—CONT'D

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS
Case 4 ³	46	0	Para 4	Deafness occurred with first pregnancy. Increased after the other three
Case 9	34	Mother, maternal grandmother, 2 cousins	Para 1	Deafness occurred with first pregnancy
Case 18	27	Paternal aunt	Para 1	Deafness increased after pregnancy
Case 21	29	Mother	Para 1	Deafness occurred with first pregnancy
2-5 ⁴	50	0	Para 7	Deafness increased after pregnancies
3-14	62	Mother	Para 3	Pregnancy did not influence hearing
L. B. ⁵	32	0	Para 2	Pregnancy did not influence hearing
Case 1 ⁶	30	0	Para 2	Deafness increased after first pregnancy. Hearing markedly improved in seventh month of second pregnancy. Deafness much worse after second delivery
Case 2	45		Para 3	Deafness decreased during last month of first and second pregnancies. Improvement disappeared after confinement. No change during third pregnancy
A. S. ⁷	22	-	Para 3	It is difficult in any way to see that pregnancy influenced hearing

³Lempert, J.: Arch. Otolaryng. 28: 42, 1938.⁴Davenport, C. B.; Milles, B. L.; Frink, L. B.: Arch. Otolaryng. 17: 340, 1933.⁵Fowler, E. P.: Laryngoscope 52: 725, 1942.⁶Ashcroft, D. W.: J. Laryng. & Otol. 50: 268, 1935.⁷Bunch, C. C.: Laryngoscope 40: 805, 1939.

in the following case reports. Better nutrition, high vitamin and mineral supplements to the diet, prompt cure of a respiratory disease and correction of metabolic defects can surely be of service to the otosclerotic patient.³⁴⁻³⁷

Timely education in lip reading and the employment of the improved type of hearing aids will do much to soften the impact of the more apparent degrees of deafness.³⁸ Safe operative cure of this condition awaits further developments along the lines of the present fenestration operation.³⁹⁻⁴¹

Conclusions

1. Our attempts to collect these data have convinced us that difficulties in hearing during pregnancy are frequently overlooked, neglected entirely, and often inadequately studied.

2. A very careful family history concerning deafness should be taken on every pregnant woman who experiences appreciable changes in hearing.

TABLE IV. CASES WITH AUDIOGRAMS (By PERSONAL COMMUNICATION)

CASE	AGE, DATE AGE, DATE OF DEAFNESS	FAMILY HISTORY OF DEAFNESS	AGE AT ONSET OF DEAFNESS	OBSTETRIC HISTORY	AUDIOGRAMS		COMMENT
					BEFORE	DURING AFTER	
H. M. B.	32	-	23	Para 1 July, 1937 Para 2	Between Sept., 1935, and Sept., 1937, there was a loss of 7 decibels in the right, and no loss in the left		"Loss of hearing normal for this length of time," Shambaugh, G.
McC.	-	-	-	Para 1 Para 2 Two pregnancies between audio-grams	Jan., 1934 R 18-25 L 36-55	June, 1938 R 22-30 L 38-60	Hayden, D. B.
D.	-	-	-	Para 1	Jan., 1938 R 19-27 L 34-50	Feb., 1939 R 17-28 L 33-60	Hayden, D. B.
S.	-	-	-	Para 1	April, 1938 R 30-48 L 21-40	March, 1939 R 46-69 L 33-63	Hayden, D. B.
H. J.	-	-	-	Para 1	July, 1935 R 15-70 L 20-90	May, 1939 R 36-90 L 50-95	Hayden, D. B.
W.	-	-	-	Para 1 Oct., 1937 Para 2 Aug., 1942			Hayden, D. B.
B.	-	-	-	Para 2 May, 1942	Oct., 1939 R 50-50 L 40-55	Feb., 1942 R 35-55 L 10-30	Hayden, D. B.
L. N. G.	-	-	-	Para 1	June, 1941 R 25-50 L 30-55	April, 1943 R 20-60 L 20-60	Hayden, D. B.
					Audiograms same before and after pregnancy		Fowler

W. W.	33 in 1942	-	22	Para 1 Sept., 1932 Para 2 Miscarriage Para 3 Oct., 1934	Jan., 1931 R 20-40 L 46-56 June, 1933 R 31-43 L 31-56	Oct., 1932 R 24-50 L 30-58 Dec., 1934 R 34-54 L 44-58 Sept., 1936 R 50-56 L 50-60 Dec., 1939 R 40-70 L 40-70	60% cases of otosclerosis af- fected by pregnancy Advises therapeutic abortion at fourth or fifth month Tobey, G. L., Jr. Irving, F. C.	
G. R. H.	-	0	-	Para 1	R 40-56 L 15-35	R 53-73 L 45-60 (5 months post partum)	Tobey, G. L., Jr.	
L. T. H.	-	0	-	Para 1 June, 1928 Para 2 March, 1932	Aug., 1925 R N-33 L 13-65 Oct., 1930 R 40-50 L 40-55	Nov., 1927 R 10-45 L 25-65 Jan., 1928 R 10-40 L 25-55 Dec., 1931 R 20-45 L 25-55	Aug., 1928 R 30-40 L 36-55 July, 1932 R 25-41 L 36-55 March, 1940 R 22-42 L 30-55	Tobey, G. L., Jr.
H. S. A.	34	Father	1932 (24 yr.)	Para 1 Jan., 1930 Para 2 May, 1932 Para 3 Nov., 1934	Oct., 1931 R 20		"Deafness noticed during sec- ond pregnancy. Increased during third. Therapeutic abortion Nov., 1934. Hear- ing improved." Friedberg, S.	
R. S.	30	Father	1 yr.	Para 1	R N L 40-48	R 0-10 L 42-48	"No appreciable change in hearing during pregnancy." Friedberg, S.	
F. A.	22	0	4 months? 2 years	Para 1	R N L 20-50	R N L 20-40 (3 mo. preg- nant)	"Hearing improved 10 decibels at 3 months." Friedberg, S. Curry, L. T.	

TABLE V. CASES WITH AUDIOGRAMS (FROM THE LITERATURE)

CASE	AGE AND DATE	FAMILY HISTORY OF DEAFNESS	AGE ONSET OF DEAFNESS	OBSTETRIC HISTORY	BEFORE	AUDIOGRAMS DURING	AFTER	COMMENT
M. S.	27 in 1937	0		Para 1 June 5, 1937	May 8 R 35-75 L 45-85		June 9 R 40-85 L 35-55 Dec. 21, 1938 D 44-70 L 30-55	"It is difficult to see in any way that definite increase in deafness has accompanied child-bearing." ¹
R. B.	21 in 1936	0		Para 1 Sept. 19, 1936	Sept. 9 R 25-65 L 15-40		Nov. 27, 1936 R 30-60 L 25-50 Oct. 5, 1937 R 25-65 L 20-45	
M. B.	23 in 1938	0		Para 1 Aug. 14, 1938	Jan. 11, 1937 R 5-40 L 5-28		Sept. 24 R 10-40 L 0-35 Jan. 14, 1939 R 10-40 L 10-35	
E. C.	24	-	-	Primipara Oct. 31, 1937		July 7 R 30-75 L 40-75	Feb., 1938 R 40-80 L 40-85	
A. J.	31	-	-	Para 2 Oct. 16, 1932	Dec., 1931 R 10-55 L 17-50		June, 1937 R 25-50 L 20-50	

¹Bunch. C. C.: Laryngoscope 49: 805, 1939.

3. For progressive deafness to be considered as an indication for therapeutic abortion a definite diagnosis of otosclerosis must first be made.

4. Definite otological evidence should be obtained and preserved before, during, and following pregnancy and lactation for evaluation concerning succeeding pregnancies.

5. Otosclerosis should probably not contraindicate marriage or a trial pregnancy.

6. Otosclerosis should not be considered as an indication for therapeutic abortion in the primipara.

7. A familial history of deafness need not be present but may be one of the deciding factors in the decision for interruption of pregnancy. We believe that a multiparous woman may have considerable right to question the continuation of her pregnancy if accurate otological evidence obtained in previous pregnancies has shown a marked, *sustained*, loss of hearing.

8. Before therapeutic abortion is decided upon, the patient should be informed that otosclerosis is a progressive disease, even without pregnancy; also that hearing aids and lip reading offer great help.

9. Fetuses in all stages of development born to mothers with decreased hearing should be preserved for examination by a competent otological pathologist. This is especially true of twin pregnancies.

I wish to express my great appreciation to the many otologists and obstetricians whose names are included in the above tables who have helped me in the preparation and compilation of this manuscript.

55 EAST WASHINGTON STREET

References

1. Kerrison, P. D.: Diseases of the Ear, Philadelphia, 1913, J. B. Lippincott Co.
2. Shambaugh, G. E., Jr.: Arch. Otolaryng. 26: 583, 1937.
3. Fowler, E. P.: Ann. Otol., Rhin. & Laryng. 45: 170, 1936.
4. Nash, C. S.: Ann. Otol., Rhin. & Laryng. 39: 769, 1930.
5. Ulrich, K.: Acta oto-laryng. 27: 505, 1939.
6. Albrecht, W.: Ztschr. f. Hals-, Nasen- und Ohrenh. 29: 55, 1932.
7. Rodin, F. H.: Arch. Otolaryng. 17: 179, 1933.
8. Shambaugh, G. E., Shambaugh, G. E., Jr.: Arch. Otolaryng. 17: 171, 1933.
9. Shambaugh, G. E., Jr.: J. A. M. A. 104: 1216, 1935.
10. Hagens, E. W.: Arch. Otolaryng. 34: 583, 1941.
11. Fowler, E. P.: Laryngoscope 52: 718, 1942.
12. Guggenheim, L. K.: Otosclerosis, published by the author, St. Louis, 1935.
13. Bland, P. B.: Practical Obstetrics, Philadelphia, 1932, F. A. Davis Co.
14. Stander, H. J.: Williams Obstetrics, New York, 1941, D. Appleton-Century Co.
15. Irving, F. C.: A Textbook of Obstetrics, New York, 1936, The Macmillan Co.
16. DeLee, J. B.: The Principles and Practice of Obstetrics, Philadelphia, 1936, W. B. Saunders Co.
17. Taussig, F. J.: Abortion, Spontaneous and Induced, St. Louis, 1936, The C. V. Mosby Co.
18. Adair, F. L., Steiglitz, E. J.: Obstetric Medicine, Philadelphia, 1934, Lea and Febiger.
19. Adair, F. L.: Obstetrics and Gynecology, Philadelphia, 1940, Lea and Febiger.
20. Shambaugh, G. E., Jr.: Arch. Otolaryng. 28: 780, 1938.

21. Despons, J.: *Bull. Soc. méd.* 41: 184, 1935.
22. Fowler, E. P.: *Ann. Otol., Rhin. & Laryng.* 42: 714, 1933.
23. Selfridge, G.: *Ann. Otol., Rhin. & Laryng.* 46: 875, 1937.
24. Bunch, C. C.: *Ann. Otol., Rhin. & Laryng.* 43: 344, 1934.
25. Davenport, C. B.: *Am. Otol. Soc., Abstract Arch. Otolaryng.* 16: 439, 1932.
26. Falta, L.: *Zentralbl. f. Hals-, Nasen- und Ohrenh.* 15: 549, 1930.
27. Weber, M.: *Ztschr. f. Hals-, Nasen- u. Ohrenh.* 26: 62, 1930.
28. Gottlieb, M. J.: *Ann. Otol., Rhin. & Laryng.* 43: 541, 1934.
29. Schmidt, E.: *Arch. f. Ohren-, Nasen- u. Kehlkopfh.* 136: 188, 1933.
30. Goerke: *Ztschr. f. Laryng., Rhin., Otol.* 23: 85, 1935. (Cited from Despons. 21)
31. Mortimer, H., Wright, R. P., Collip, J. B.: *Canad. M. A. J.* 35: 615, 1936.
32. Griefenstein: *Ztschr. f. Hals-, Nasen- u. Ohrenh.* 46: 344, 1939.
33. Jones, I. H.: *Laryngoscope* 49: 505, 1939.
34. Guggenheim, L. K., Gunther, L., Goodhill, V., Irvine, M.: *Arch. Otolaryng.* 34: 501, 1941.
35. Covell, W. P.: *Laryngoscope* 51: 683, 1941.
36. Bauer, M.: *Monatschr. f. Ohrenh.* 75: 22, 1941.
37. Selfridge, G.: *Arch. Otolaryng.* 34: 125, 1941.
38. Berry, G.: *Laryngoscope* 42: 615, 1942.
39. Shambaugh, G. E., Jr.: *Arch. Otolaryng.* 36: 23, 1942.
40. Lempert, J.: *Arch. Otolaryng.* 27: 555, 1938.
41. Campbell, E. H.: *Laryngoscope* 52: 593, 1942.

Discussion

DR. BAYARD CARTER, DURHAM, N. C.—Dr. Allen has given a comprehensive survey of the literature which shows that otosclerosis in females constitutes 66 to 79 per cent of reported case records. He also shows how the problem of otosclerosis of pregnancy was approached in Germany and France. In Germany, the treatment of the disease in pregnancy was based upon political ideology, i.e., race betterment; in France, the treatment was based upon the religious concept. Medical care of the patients, therefore, has been tinted with one of these concepts.

A reading of this paper also shows the confusion existing concerning etiological ideas of the disease. That the disease may be caused or aggravated by head colds, faulty diet, poor teeth, faulty metabolism, puberty, by pregnancy and lactation, menopause, by total sterilization and by mental disease, is considered in the review. The validity and nonvalidity of hereditary studies are also discussed. The author advances the theory that the high estrin levels which occur during pregnancy may affect the hearing by their effects upon the mucous membrane of the ear in a manner similar to the action of the high estrin levels on mucous membranes in other parts of the body. This theory is an arresting one and worthy of serious consideration.

Dr. Allen also expresses clearly the criteria for diagnosis, i.e., progressive deafness, Bezold's triangle, normal middle ear and eustachian tube. He rightly emphasizes the necessity of audiometer measurements of the loss or gain in hearing to make case records reliable and complete.

Our experience with otosclerosis in pregnancy is based upon the study of two patients. One of these patients had a complete and comprehensive work-up and one had incomplete study.

PATIENT 1.—Aged 23, para 0-0-0. The mother of this patient was deaf. The patient herself was "hard of hearing from 13 years of age and the diagnosis of otosclerosis was made prior to marriage." This patient presented herself with a pregnancy of eight weeks. She and her husband were highly intelligent and asked advisability of abortion. This we declined to do and explained that the advantages of children, who would probably not have otosclerosis, would far outweigh an increase in her deafness.

The first pregnancy, 11 years ago, was normal in every way and the child was normal. The audiometer tracing, however, showed a decrease in hearing.

The second pregnancy, eight years ago, was also normal, but the audiometer tracing again showed a decrease in hearing.

The third pregnancy, seven years ago, ended in a spontaneous abortion at ten weeks without change in audiometer tests.

The fourth pregnancy was also normal in every way. The audiometer tests showed decreased hearing with tinnitus accentuated. This patient was last seen 15 months ago.

PATIENT 2.—Aged 36, para 9-2-7. This patient, who had noticed increasing deafness after her fourth pregnancy, was admitted for intrapartum bleeding. A spontaneous delivery and uncomplicated puerperium followed. She left the hospital against advice on the sixth day, before audiometer tests could be undertaken. A letter from the patient reported hearing “just as bad as ever but no worse.”

Dr. Allen's presentation should arouse interest concerning deafness in pregnancy and the survey as conducted by him establishes data of real clinical value.

DR. WILLARD R. COOKE, GALVESTON, TEX.—While otosclerosis is somewhat rare, to the patient concerned it is of vital importance. It behooves us not to neglect the thorough study of every case in which the disease is known to exist in the individual or in the family, or in which the rather frequently encountered symptoms of tinnitus or diminished acuity of hearing develop during pregnancy.

As a personal contribution, I can cite only two cases and a family record covering four generations. In one of the cases, no subjective change occurred during or within three years after pregnancy. In the other, the disease was markedly progressive during pregnancy without subsequent regression. The family record is as follows: The first known case occurred in the great-grandmother of the present youngest generation. Of two sons and a daughter, the daughter only was affected. The disease has not occurred in the descendants of the sons. The daughter had two sons and two daughters, one of each being affected. Neither daughter had children, and in the six children, now aged 26 to 35, of the two sons the disease has not yet appeared.

DR. FRED L. ADAIR, CHESTERTON, IND.—It seems to me that we must base our decisions on the termination of pregnancy for otosclerosis on some definitely defined ideas about abortion in general. One has to recognize in setting up indications for abortion, first the effect on the mother, and second the possible effect on the fetus in allowing the pregnancy to go on to term. Hereditary aspects are probably a factor in the condition, but the hereditary trend is certainly not 100 per cent. Are we justified in therapeutic abortion when the hereditary factor does not involve 100 per cent of the fetuses? In other words, if we do a therapeutic abortion where the hereditary factor might produce 50 per cent or less of defective offspring, we would run an even chance of destroying a normal fetus, or one which might have some defect later.

Second, are we justified in doing a therapeutic abortion where the fetus if it survives and develops the hereditary condition, though handicapped, can still lead a useful existence? In setting up an indication for therapeutic abortion that should be given serious consideration.

With regard to the mother, it is uncertain whether or not the continuation of the pregnancy really has a serious effect on the course of the disease. It certainly does not have a serious effect in all mothers. In some cases we do apparently have a temporary exacerbation of the disease which in some patients disappears after the pregnancy is over. We have difficulty in predicting in advance what effect pregnancy may have in a given case.

Then we also have to consider the very serious ethical question of whether or not some handicap to the mother, which does not interfere with her living a useful though handicapped life, justifies destroying another life which could be a perfectly normal individual.

We have to be extremely careful in setting up indications for therapeutic abortion, which get into the literature and are difficult to eradicate. This is particularly

true for conditions about which we are not clear in our own minds as to their hereditary character or their response to pregnancy. Dr. Allen's contribution has been extremely sound and sane, for this is a condition of considerable interest to the obstetrician because of the attitude of a considerable number of patients toward the condition of the child and toward their own impaired hearing.

DR. CURTIS F. BURNAM, BALTIMORE, MD.—I have had the opportunity through the Otolaryngological Department of the Johns Hopkins Hospital to consult with Dr. Samuel Crowe about the cases of clinical otosclerosis occurring there. Apparently, it is a rare disease but otosclerotic pathological changes in various parts of the temporal bone are extremely common, and where they made serial sections, a very high percentage of those bones showed the lesion. If the stapes is not involved, there is no change in hearing, and these changes have no clinical significance. Heredity, while a factor, does not justify clinical abortion, nor does the possible increase in deafness in the mother justify this procedure.

DR. JOSEPH L. BAER, CHICAGO, ILL.—Dr. Allen's note of warning brought to my mind a patient who, following her first pregnancy, had lost approximately one-third of her hearing capacity in both ears, and who deliberately embarked upon a second pregnancy, having been told that there was a distinct likelihood of further impairment of her hearing. Following the second pregnancy, she had lost two-thirds of her hearing and was resorting to mechanical devices. She and her husband consulted with me concerning the advisability of a third pregnancy. I pointed out that it might terminate in complete deafness, which opinion was confirmed by the otologist. Nevertheless, she deliberately embarked upon a third pregnancy and did, in fact, lose almost her entire hearing perception. Now if she had inadvertently become pregnant on this third occasion and had appealed to me for termination of that pregnancy, because of what had happened previously, I would have had no hesitation about performing a therapeutic abortion and sterilization.

DR. ALLEN (closing).—I have nothing to add except in replying to the question about the diagnosis of otosclerosis by x-ray. My otological friends have made it very plain to me how difficult it is to make a definite diagnosis by the ordinary tests, and in all the literature I have read I have seen no mention of diagnosis by x-ray.

A THERAPEUTIC REGIMEN FOR ECLAMPSIA*

Based on a Personally Conducted Series of 142 Consecutive Cases
Without a Maternal Fatality

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ECLAMPSIA still constitutes a major obstetric problem. Its incidence and mortality rate, although they vary throughout the country, remain on the average appallingly high. It was responsible for more than a third of the total maternal deaths in the six state hospitals of Louisiana during 1943, and the case fatality in the 161 cases treated in these institutions during that year was approximately 10 per cent (16 deaths).

As far as I am able to ascertain from the voluminous literature, the 142 consecutive cases of eclampsia which I am reporting in this communication constitute the largest single series on record without a fatality. The material consists of 120 cases of eclampsia treated under my personal supervision and direction at Charity Hospital of Louisiana at New Orleans during the five-year period ending January 1, 1944, and of 22 cases treated during 1941 at the Pineville Charity Hospital, with the cooperation of Dr. John W. Williams. As there are no essential differences in the material, it will hereafter be analyzed as a unit.

Although, as already stated, these cases were treated under my personal supervision and direction, their uniformly successful outcome is due to the enthusiasm and warm cooperation of the visiting and resident staffs of Charity Hospital, including Dr. Frank J. Bertucci, Dr. William F. Guerrero, Dr. Daniel W. Goldman, Dr. Ben L. Lehman, Dr. Roland F. Phillips, Dr. Stephen L. Watson, and Dr. John W. Williams, the latter of whom later transferred to the Pineville Charity Hospital. I am happy to acknowledge their share in this work, which many times required the continuous observation of patients, sometimes by several members of the staff, for hours on end. Such observation, as I shall point out later, had much to do with the successes achieved.

All of these cases were treated by the same general, essentially conservative plan, which was, however, modified to meet the circumstances of every individual case. We are convinced that the universal adoption of a similar individualized but essentially conservative therapeutic regimen would materially reduce the general mortality in this disease. A review of the recent literature supports the point of view that the therapy of eclampsia is still unsettled. The chief point of similarity

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in the various plans now advocated is that they tend to be less radical than they formerly were, but there, as a rule, resemblances end. My own experience with interns, residents, postgraduate students and even practicing physicians has convinced me that this lack of agreement on the part of obstetric authorities results in confusion and experimentation among inexperienced men, many of whom, although well taught, seem inclined to regard eclampsia as an etiologic problem rather than as a clinical condition in which two lives are the stake. Personally, I have no doubt that this state of confusion contributes heavily to the general mortality of the disease.

Analysis of Material

The principal object of this communication is to outline a plan of therapy for eclampsia, the effectiveness of which has been demonstrated in the series of cases under consideration. The use of special personal records in these cases, however, in addition to the usual hospital records, has resulted in the accumulation of considerable other data of interest, which will be briefly summarized.

Incidence.—During the five-year period in which these 142 cases were treated, the incidence of toxemia of all degrees and types in the wards in my charge was 8.12 per cent, and eclampsia represented 13.1 per cent of all the toxemias observed. This relatively high proportion is chiefly explained by the fact that as a rule only severe cases of toxemia reach the hospital from distant areas. Patients with mild degrees seldom leave rural areas for medical attention, and do not always seek it even if they live in the city. It should be added, however, that approximately 75 per cent of all patients now delivered in the New Orleans Charity Hospital have received prenatal care in the hospital clinics.

✓ The incidence of eclampsia on my service during this period was 1.07 per cent, the ratio being 1:93.3 viable obstetric admissions. The ratio varied from 1:98 in 1939 to 1:103 in 1943. It was 1:94 in 1940, 1:79 in 1941, and 1:105 in 1942. Failure to demonstrate a uniformly declining incidence curve is not altogether discouraging, for it is to be explained by improvement in hospital facilities, as the result of which patients from distant areas are now adding materially to local statistics. Approximately 60 per cent of the patients in this series resided outside of the city limits, and 12 per cent lived more than 50 miles away.

The marked disproportion in the racial incidence (114 colored to 28 white patients) is more apparent than real, since the incidence rate of eclampsia, based on obstetric admissions, was almost the same for the two races (1.05 per cent colored, 1.08 per cent white). Comparisons on the basis of race are frequently interesting and valuable at the New Orleans Charity Hospital, but in eclampsia we have observed no inherent racial variation effective in influencing either the susceptibility to, or the severity of, the disease. We have also observed no difference in eclampsia as exhibited in rural and urban Negro women, or in southern and northern Negro women.

This series bears out the common observation that eclampsia is definitely a disease of young primiparas. Although the age range was

from 13 to 41 years, 71 per cent of the patients (101) were less than 21 years of age. Although the parity ranged from one to 10 pregnancies in the 26 multiparas in the series, 81.2 per cent of the patients (116) had not previously been pregnant, and only four patients had had more than two pregnancies. On the other hand, the disease tended to be more severe in older women and in multiparas, probably because repeated childbearing had lowered resistance and initiated tendencies to chronic vascular or renal disease.

Eclampsia is most likely to occur in the third trimester of pregnancy. In one case in this series it developed at 26 weeks, in another at 28 weeks, and in a third at 30 weeks, but 38 per cent of all cases occurred between the thirtieth and thirty-sixth weeks, and 60 per cent between the thirty-sixth and fortieth weeks.

Possible Etiologic Factors

Special studies were made of certain factors to determine their possible etiologic significance. In this series, as in all other reported series, convulsions were usually precipitated in susceptible cases by such generally recognized stimuli as anger, worry, overwork, lack of sleep, the irritation of examinations and other manipulations, or the stress and strain of labor and delivery. No fundamental emotional instability, however, was evident in any patient. As a matter of fact, when once the stage of acute toxemia had been controlled, these women, as a rule, seemed to be rather more stable emotionally than are the average pregnant women.

Meteorological Environment.—In some instances, particularly of antepartum eclampsia, there was no apparent reason for the abrupt onset of the attack. Our own experience, like that of other obstetricians, is that eclampsia tends to occur in groups of cases, after long intervals without a case. Recently, for instance, following an interval of six weeks without a single case, seven women with eclampsia were admitted within 30 hours to three state hospitals located within a radius of 150 miles. Intrinsic or extrinsic factors would scarcely operate simultaneously, and chance coincidence seems an unlikely explanation.

Since local atmospheric changes seem to furnish the only obvious common factor in such circumstances, an investigation from this standpoint was undertaken in all cases of antepartum eclampsia in this series. Through the cooperation of the U. S. Weather Bureau in New Orleans, meteorograms made at the time of onset of the seizures were studied in these cases, and it was found that in 83 per cent (62 cases) the onset coincided with a rising barometric pressure, a decreasing environmental temperature, and a high degree of humidity. In six instances tropical electrical storms were also present. We have, of course, no intention of claiming that the weather is of etiologic significance from the standpoint of the disease itself, but the speculation seems reasonable that abrupt changes in the physical milieu sometimes may require physiologic adjustments beyond the capabilities of abnormal individuals.

Protein Deficiencies.—Dietary investigations carried out in the last 62 cases in this series suggest that protein deficiencies may be of etiologic significance in eclampsia. Certainly these studies discredit still further

the belief, which is still held in some quarters, that high protein consumption is a cause of eclampsia and that limitation of the protein intake may prevent it.

Not one of these 62 patients had an optimum protein intake (1.5 Gm. per kg. of body weight per day) and only three had an intake above the minimum subsistence level (0.75 to 0.90 Gm. per kg. per day) for the last trimester of pregnancy. The range of intake was from 0.20 to 0.92 Gm. per kg. per day, and approximately a third of the protein ingested was derived from cereal and vegetable sources and was therefore of low biologic value. In many instances, inadequacies which had apparently existed over long periods of time were aggravated during pregnancy by restriction of meat, eggs and milk, either self-adopted or carried out on medical advice. Protein deficits were also increased by such obvious causes as vomiting, frequent catharsis, and proteinuria.

Serum protein determinations made during the eclamptic stage in 47 patients showed an average concentration of 5.10 ± 1.10 Gm. per cent, in spite of hemoconcentration at the time, which is definitely lower than the normal average (approximately 6.5 Gm. per cent). A rough correlation existed between the degree of edema and the serum albumin level, but otherwise it was not possible in the individual case to correlate the serum protein level or the degree of edema with the protein intake, or to correlate this level with the degree of edema.

Cerebral Dysrhythmia.—Electroencephalographic studies on 26 patients who had had eclampsia from two days to four and a half years previously revealed abnormal findings in only three, 11.5 per cent, which is approximately the incidence of abnormality likely to be found in any series of similar tests on apparently normal individuals. The patient who had had eclampsia two days before, and the patient who had had eclampsia in two successive pregnancies were both normal. The findings thus do not support the theory that eclamptic subjects may suffer from a primary cerebral dysrhythmia, which may be exaggerated to the convulsive degree by a "trigger mechanism" in the form of the associated toxemia.

Convulsive Diathesis.—The familial tendency to eclampsia postulated by certain observers on the basis of small numbers of observations is not borne out by this study. Four of the 26 multiparas in the series had previous histories of toxemia. One patient had eclampsia in 2 successive pregnancies during the period of observation, 1 had a previous history of eclampsia, and 2 had had severe pre-eclamptic toxemia in previous pregnancies. The apparent rate of repetition, however, 16.6 per cent, decreases to 6.7 per cent when the 60 pregnancies in these 26 women are taken into consideration. Excepting the two instances of eclampsia, not a single patient gave a history of previous convulsive disorders of any kind.

The family history is complete in only 46 of the 142 patients. The mother of one patient and the sister of another had had eclampsia, and the brother of a third patient suffered from epilepsy. It is a matter of interest, however, that twin sisters of two of the eclamptic subjects were normal, as were the families of the two patients with recurrent eclampsia. The family history was thus positive in only 6.5 per cent of these 46 cases, and even when the two patients with a personal history of recurrent eclampsia are added to the group of positive subjects, the familial incidence rises to only 10.8 per cent.

The constitutional build of eclamptic subjects seems to play some part in the development of the disease, although our observations on this point are incomplete. The weights of 68 patients as determined at the first postpartum visit ranged from 88 to 263 pounds. Several weighed less than 100 pounds, but the average weight was 145 pounds, and 17 weighed more than 160 pounds. Quite aside from statistical data, we, like others, have learned to treat with particular respect the thick-necked eclamptic subject of short stocky build.

Complications of Pregnancy.—Complications and abnormalities were frequent in this series, though whether they were causal or merely coincidental it is not possible to say. Seventeen patients had syphilis and 2 had fibroids, which is about the usual incidence for these conditions on the obstetric service. Eight patients exhibited severe anemia, in one instance of the sickle-cell variety. Eleven patients (7.7 per cent) had pyelitis, which is approximately three times the clinic average. Fifteen (10.5 per cent) had hyperemesis gravidarum, which is 10 times the average. Eight (5.6 per cent) had repeated periods of vaginal bleeding, which is several times the clinic average. There were 7 sets of twins in this series, a ratio of 1:20.3, which is 4 times the average rate and which substantiates the common observation that eclampsia is unusually frequent in multiple pregnancy.

Classification and Grading

In 104 of these 142 patients, 73 per cent, convulsions began prior to delivery, and in 74 cases, 52 per cent, labor had not yet begun. Doubtful cases were classified as intrapartum if delivery occurred within 12 hours of the first convulsion. The incidence of postpartum eclampsia is unusually high because 12 patients were admitted in convulsions after delivery outside of the hospital.

If therapy is to be evaluated with any degree of accuracy, eclamptic patients must be graded on the basis of severity, as well as classified as to time of occurrence. For grading purposes we prefer the criteria proposed by Dieckmann, which are based on the presence of one or more of the following findings: (1) more than ten convulsions; (2) coma; (3) hyperpyrexia; (4) pulse rate over 120 per minute; (5) respiratory rate over 40 per minute; (6) cardiovascular impairment; (7) failure to respond to treatment. On the basis of these criteria (Table I), 52 patients (36.6 per cent) were classified as having severe grades of eclampsia. The proportion of severe grades was only about a third as high in the delivered as in the undelivered groups, but was much higher in multiparas than in primiparas (54 and 33 per cent, respectively).

TABLE I. CLASSIFICATION OF 142 CASES OF ECLAMPSIA

TYPE	NUMBER	PER CENT	GRADE			
			MILD		SEVERE	
			NUMBER	PER CENT	NUMBER	PER CENT
Antepartum	74	52.1	40	54.0	34	46.0
Intrapartum	30	21.1	18	60.0	12	40.0
Postpartum	38	26.8	32	84.2	6	15.8
Total	142	100.0	90	63.4	52	36.6

Such grouping, though very useful, is sometimes difficult and is frequently inaccurate, for patients who present apparently identical manifestations may actually be quite dissimilar in their reactions to the disease. One patient, for instance, without ever seeming very seriously ill, may recover in spite of a dozen or more convulsions, oliguria, hyperpyrexia, and very rapid pulse and respiratory rates, while another may seem critically ill in the absence of most or all of these manifestations. When tangible as well as intangible factors are taken into consideration, the incidence of severe grades of eclampsia in this series rises from 36.6 to 44 per cent.

The number of convulsions ranged from one to 22, and 19 patients (13.4 per cent) had more than 10. Although the number is generally an index of the severity of the disease, one patient in this series who had 22 convulsions delivered a live baby and has presented no abnormal sequelae.

Experience with many patients whose lives were jeopardized by severe pre-eclamptic toxemia has caused us to speculate on the possibility that convulsions may sometimes form an actual protective or release mechanism which guards against even greater dangers. Not infrequently, toxemic patients appear in better condition and seem more easily managed following a short seizure than before it occurred. Furthermore, critically ill toxemic subjects with no tendency to convulsions may present greater residual damage than true eclamptic subjects. This reasoning is in line with the accepted fact that eclampsia without convulsions is the most dangerous type of the disease. Paradoxical as the theory seems, it is not incompatible with accepted explanations of other defense mechanisms, such as the development of fever and leucocytosis in infection and of hypotension and shock in ruptured ectopic pregnancy.

Plan of Therapy

The plan of therapy outlined in this paper is based not only on our experiences in the 142 cases reported herewith, but also on a personal experience of approximately 250 other cases which have come under my observation in the past 14 years. The basic principles have been evolved gradually, but have not been changed substantially in the last two years.

There is nothing new or original about this therapeutic regimen. The various steps have been proposed by others and are well known. Many have secured excellent results with them. Others have failed, chiefly, we believe, because the treatment is superficially simple and unspectacular, as well as exceedingly tedious, and as a result two precautions to the strict observance of which we attribute much of our success are likely to be omitted:

1. Constant (in the most literal sense of the word) observation of each eclamptic patient by an experienced staff throughout the entire course of treatment, which permits

2. Careful integration of the various therapeutic components into an individualized regimen rather than their application as a standard routine of treatment.

The basis of the whole regimen is an ultraconservative concept of management, in which the dangers of overtreatment and indiscriminate treatment as well as those of undertreatment are evaluated.

The outline of treatment which follows is deliberately detailed and may seem unnecessarily so in comparison with other plans in which some special phase of therapy is stressed. We regard strict attention to details, however, as fundamental to success, for, as already pointed out, individual differences among patients make routine orders unsafe and continuous observation mandatory, in order to determine the changing indications for therapy. It is impossible to outline a safe treatment for the entire course when the patient is first seen, and seldom possible prior to delivery.

For clinical purposes, the therapy of eclampsia is best planned according to the stage of the disease. For this purpose eclampsia may be arbitrarily divided into the following stages, which may vary widely or be absent and all of which, for obvious reasons, occur only in antepartum eclampsia:

1. *The Convulsive Stage*.—This is the interval from the onset of convulsions to their complete control. It is characterized clinically by convulsive seizures, by hyperirritability alternating with coma, and by stupor and disorientation.

2. *The Postconvulsive Stage*.—This is the interval between the final convulsion and the return of full consciousness. It is characterized clinically by coma, semicoma and restlessness, but convulsions are absent.

3. *The Controlled-Eclamptic Stage*.—This is the interval of convalescence and improvement between the postconvulsive stage and the onset of labor. There may be during it an occasional abrupt recurrence of fulminating symptoms, but it is usually characterized by definite amelioration or complete disappearance of acute toxic manifestations.

4. *The Postecclamptic-Parturient Stage*.—This stage includes the period of labor and delivery.

5. *The Postecclamptic-Postpartum Stage*.—This is the period between delivery and the patient's discharge from the hospital.

Although only five formal stages of eclampsia are recognized, it is well to emphasize at this point that the eclamptic woman should be observed for a long period in the postpartum clinic and should not be discharged from observation during the remainder of her life. Adequate supervision and care are particularly essential during subsequent pregnancies. •

The Management of the Convulsive Stage

Antepartum eclampsia naturally is the most difficult to manage because the problem of termination of pregnancy is added to the purely medical problem involved in the eclamptic state. For this reason, the plan of management which follows deals primarily with this type; the same principles, however, are applicable to all types.

In the convulsive stage the following measures are employed:

1. *General and Special Measures.*—The patient is put to bed in a quiet, darkened room and medical and obstetric examinations are, so far as possible, deferred until sedation has become effective, since even apparently insignificant manipulations may precipitate further convulsions.

During convulsive periods and periods of coma the patient is protected against falls and other injuries, preferably by bed guards or side boards. We have observed two instances of cerebral concussion and one of intracranial hemorrhage, as well as several serious contusions and lacerations, because these simple precautions were omitted. Forcible restraints, however, are highly irritating and should never be employed.

False teeth, rings, bracelets and other jewelry are removed at once. A mouth gag is inserted, with due care that neither the patient nor the attendant is injured in the process. We have observed serious hemorrhage from lacerations of the tongue and lips because this precaution was omitted. If the tongue falls back and interferes with breathing it is pulled well forward, and, if necessary, is held in that position.

The patient's position in bed is important. Pillows are not used, but the head of the bed is elevated unless pulmonary edema is so extreme as to demand postural drainage by elevation of the foot of the bed. At least once each hour the entire body is gently shifted from one position to another. A suction apparatus with attached catheter is employed without delay to aspirate vomitus, blood, mucus, and fluid originating in pulmonary edema. Pure oxygen is administered by continuous flow through a nasal catheter or, if cyanosis is marked, by means of a mask. These measures, all of which promote respiratory ease, will usually prevent such common pulmonary complications of eclampsia as respiratory distress, cyanosis, inspiration atelectasis, pneumonitis, pneumonia, and, above all, pulmonary edema.

The blood pressure cuff is kept continuously on the arm and the blood pressure is determined hourly until convulsions and coma are completely controlled. A retention catheter is inserted in the bladder and the urinary volume is determined hourly. The catheter is also inspected regularly for possible leaks or kinks and is irrigated every four hours to prevent obstruction by pus or by precipitates of protein, which frequently accompany or follow periods of oliguria or anuria.

The blood is typed as soon as possible, since transfusion may be required at any time to combat anuria, shock developing from vascular collapse, hemorrhage from abruptio placentae or placenta previa, postpartum hemorrhage, or any other of the complications not infrequently associated with eclampsia.

2. *Sedation to Control Convulsions.*—As soon as the patient is admitted to the hospital, morphine sulfate gr. $\frac{1}{4}$, and sodium phenobarbital gr. 5, are given subcutaneously. Fifteen minutes later, if convulsions are still present or if hyperirritability is extreme, she is also given 20 c.c. of 10 per cent magnesium sulfate solution, which is injected slowly into the vein. In our experience intramuscular injection is less effective than intravenous injection.

Magnesium sulfate sometimes has a favorable effect on cerebral edema and may stimulate urinary output. If in spite of these measures severe convulsions persist, as they occasionally do, sodium amytal is given intravenously in doses of 3 to 6 gr., or morphine is repeated in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain. Magnesium sulfate is not repeated unless convulsions recur

or seem imminent, possibilities which are guarded against by continued sedation, usually in the form of sodium phenobarbital (gr. 1.5 to 5, as necessary to control restlessness).

It will be observed that we use all sedatives in very small doses and that we limit the list, as far as possible, to morphine, sodium phenobarbital, and magnesium sulfate. This is intentional. Sedatives are administered in the smallest amounts sufficient to terminate convulsions, prevent their recurrence, and control extreme irritability, on the principle that deficits in sedation can be rapidly and easily corrected, but that oversedation cannot be withdrawn.

The rationale of strict limitation of sedation is clear. Our own observation of eclamptic cases in which heavy sedation is used is that the blood pressure is lowered to dangerous levels; anoxemia, anoxia and acidosis are aggravated by diminution of respiratory activity; the tendency to cerebral and pulmonary edema is increased; stupor and coma are accentuated; and the urinary output is decreased. As a result, patients in profound drug stupor may develop serious complications, which may prove resistant to therapy. Heavy sedation also affects the child adversely.

A second reason for using a limited number of drugs, and those in small quantities, is the considerable variation both in eclampsia and in the individual patient's idiosyncrasy to drugs. A third is that there may have been a previous administration of drugs in the home, on the way to the hospital, or in the admission room, which for various reasons may not be realized until later. We have seen patients remain in profound stupor for as long as 96 hours, apparently from the cumulative action of various drugs administered at short intervals.

The principles outlined were applied in the 142 cases in this series. Fifty-five patients (32 per cent) received only morphine and sodium phenobarbital, and 76 (54 per cent) also had one or more injections of magnesium sulfate. Only 12 patients (14 per cent) had sodium amytal, always in small doses, and this drug was used only twice in the last 51 cases.

The success of these measures is evident in the rapid and complete control of convulsions achieved by them. Forty per cent of the patients (57) in this series had no more convulsions after treatment had been instituted, while 34 per cent (48) had only one more (Table II). Within 30 minutes after treatment had been started, convulsions were permanently controlled in more than half the patients (Table III). Response to therapy was usually most rapid in postpartum and least rapid in antepartum eclampsia, but in no instance did patients in the antepartum

TABLE II. RESPONSE OF CONVULSIONS TO THERAPY

	TYPES OF ECLAMPSIA						CUMULATIVE PER CENT
	ANTEPARTUM		INTRAPARTUM		POSTPARTUM		
	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	
None after institution of treatment	20	27.0	3	10.0	34	89.6	40.1
One convulsion	33	44.6	12	40.0	3	7.8	73.9
Two convulsions	5	6.8	11	36.7			85.2
Three convulsions	5	6.8	3	10.0			90.8
Between 3 and 5 convulsions	7	9.4	1	3.3	1	2.6	97.1
Between 5 and 10 convulsions	3	4.0					99.3
More than 10 convulsions	1	1.4					100.0
Total cases	74	100.0	30	100.0	38	100.0	

group have recurrences of their convulsions after delivery. Such recurrences as did develop came on early and suddenly, but were usually mild and of short duration.

TABLE III. TIME REQUIRED TO CONTROL CONVULSIONS

	TYPES OF ECLAMPSIA						CUMU- LATIVE PER CENT
	ANTEPARTUM		INTRAPARTUM		POSTPARTUM		
	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	
None after institution of treatment	20	27.0	3	10.0	34	89.6	40.1
Within 30 minutes	12	16.2	5	16.7	1	2.6	52.8
Within 45 minutes	15	20.3	7	23.3	1	2.6	69.0
Within 60 minutes	9	12.1	9	30.0	2	5.2	83.1
Within 2 hours	10	13.5	3	10.0			92.3
Within 4 hours	3	4.0	2	6.7			95.8
Longer than 4 hours	5	6.8	1	3.3			100.0
Total cases	74	100.0	30	100.0	38	100.0	

3. *Verification of Diagnosis.*—Convulsions, regardless of their origin, can all be controlled by the same therapeutic measures, but additional treatment without an exact diagnosis may end in disaster, for pregnancy plus convulsions does not always add up to eclampsia. We once saw a pregnant woman with diabetic convulsions treated with glucose and another with postconvulsive shock and a ruptured uterus treated as if she were in eclamptic coma, with disastrous results in both cases. The diagnosis of eclampsia can be made with reasonable accuracy in most cases by careful interpretation of the sequence of events as correlated with hypertension, edema, and proteinuria.

During the five-year period of this study, 162 women with convulsions were admitted to our obstetric services in the New Orleans Charity Hospital, but only 120 of them had eclampsia. The remaining 42 patients presented variously:

Epilepsy in 11 cases.

Central nervous system affections in five cases (brain tumor, specific meningitis, arsenical encephalitis, traumatic concussion, and rupture of a syphilitic basilar aneurysm).

Hysteria and diabetes in four cases each.

Reactions to therapeutic measures in four cases (blood transfusion, caudal analgesia, intravenous oxytocic medication, barbiturate analgesia).

Hematogenous disease in three cases (massive septicemia, massive hemorrhage, hemolytic crisis in sickle-cell anemia).

Chronic hypertensive disease (encephalopathies) in three cases.

Chronic renal disease (glomerulonephritis, pyelonephritis, renal calculi) in three cases.

Food poisoning and drug poisoning in one case each.

Hyperemesis gravidarum, chorea, and tetany and alkalosis in one case each.

4. *Measures to Promote Hemodilution, Diuresis and Detoxification.*—

As soon as the diagnosis of eclampsia has been confirmed, 500 c.c. of 20 per cent dextrose solution in distilled water are given by intravenous infusion, the period of administration usually covering about 50 minutes. A patient with evidence of cardiac failure or pulmonary edema receives from 50 to 150 c.c. of 50 per cent solution, and a patient with evidence of dehydration, which may be present in spite of edema, receives 1,000 c.c. of 5 to 10 per cent solution. If the initial injection fails to stimulate

a satisfactory urinary output, the concentration of the solution is increased and the volume is decreased, but infusions are seldom given oftener than every four hours. If the urinary output at the end of four hours has averaged less than 25 to 30 c.c. per hour, an infusion of 300 c.c. of 30 per cent dextrose solution is given. Thus the intravenous administration of dextrose is carried out in all cases only during the period the patient is unable to take sufficient fluids by mouth, and it is discontinued if it is clearly producing no results.

Although the value of intravenous injections of hypertonic dextrose solutions in promoting hemodilution and diuresis has long been established, it is our custom to use them only on strict indications. They are employed chiefly during the convulsive stage, and they are limited to the smallest amounts which will produce a urinary output of 25 to 30 c.c. per hour. The injudicious use of large quantities of fluid may result in cardiac embarrassment and serious acute pulmonary edema, and will aggravate an already impaired water balance if there is little or no urinary output, particularly if the patient is heavily sedated.

Persistent oliguria or anuria associated with such conditions as anemia, hypoproteinemia, or hypotension due to vascular collapse or hemorrhage, demands special additional measures. Anemia and hypotension are treated by blood transfusions. Hypoproteinemia without anemia is treated by plasma transfusions. Patients who continue oliguric or anuric in spite of these measures are treated by diathermy over the kidney regions and are also given 1,000 c.c. of sodium sulfate (4.285 per cent) by vein, followed in four hours by the intravenous injection of 50 c.c. of 50 per cent dextrose. In 16 cases in this series, 9 of which were instances of intrapartum eclampsia, anuria developed for periods ranging from 8 to 31 hours.

Only 7 of the 142 patients did not receive dextrose. Seventy-five (53 per cent) received only 20 per cent solutions, but 39 (27 per cent) also received 30 or 50 per cent solutions, and 21 (15 per cent) required infusions of 5 to 10 per cent solution in addition to the higher concentrations before a satisfactory urinary output was established. Sucrose was used in four of the early cases in this series, but was discontinued, in spite of apparently satisfactory results, on the basis of reports from elsewhere of hemorrhagic nephritis following its use. Twenty-three patients (16 per cent) received blood transfusions, which in one instance amounted to 2,850 c.c., 4 received plasma transfusions, and 7 received sodium sulfate solution.

5. *Special Therapeutic Measures.*—If marked cerebral irritation is evident, in spite of sedation and intravenous dextrose therapy, spinal drainage is carried out. We have found this measure of some value, particularly in postpartum eclampsia, in the reduction of intracranial pressure due to spasm, edema or hemorrhage, as well as in the verification of the diagnosis of hemorrhage, but we are opposed to it as a routine. Spinal drainage was employed in 12 patients in this series, in 4 of whom it was used twice, and in 1 of whom it was used three times. We are also opposed to venesection, even in the presence of pulmonary edema.

Although in the presence of acute cardiac failure drugs of the digitalis group are theoretically of at least temporary value, we have found them of no particular benefit in the few cases in which we have used them. Toxemic subjects are unusually sensitive to them, and the vomiting which often follows their administration is undesirable. We do not use mercurial diuretics, nor do we use vasodilator drugs such as veratrum viride, the nitrites, and nitroglycerin.

The Management of the Postconvulsive Stage

The coma or semicoma which follows the final convulsion usually passes over imperceptibly into a period of stupor and lethargy, punctuated with episodes of hyperirritability and ending in gradual clinical improvement. It is only occasionally possible to demonstrate the limits of the convulsive and the postconvulsive stage because both control of convulsions and clinical improvement must be demonstrated by developments. Although too little attention is, as a rule, given to it, the postconvulsive stage is not free from danger in itself, and its dangers are increased by the too free use of hypnotic drugs and the induction of labor immediately after convulsions have ceased. The latter error, which is based on the belief that the control of convulsions is equivalent to the control of eclampsia, is a common and very dangerous mistake.

The following measures are employed in sequence during the postconvulsive stage:

1. *General and Specific Measures.*—Constant observation is continued and a quiet, restful environment is maintained. The use of nasal oxygen is continued, and material is aspirated from the throat when necessary, though the same object can be achieved in a conscious subject by instructing her to cough at frequent intervals. The head of the bed is further elevated and the height is changed at frequent intervals. This simple measure seems to improve cerebral circulation. If the patient is still unable to move about herself, her position is changed by an attendant.

Blood pressure and urinary output are determined at hourly intervals, as during the first stage, but in the absence of special indications other clinical information is obtained at four-hour intervals. As soon as is feasible in this stage, a thorough obstetric examination is concluded.

To hasten detoxification a large dose of magnesium sulfate is given by mouth; and is followed in four hours by a cleansing enema.

2. *Sedation and Administration of Fluids.*—Sodium phenobarbital in doses of 1.5 to 3 gr. is given at three- to six-hour intervals, which is usually sufficient to prevent the recurrence of convulsions. Spastic twitchings, particularly of the fingers and eyelids, often precede convulsions and indicate the need for additional sedation, but some degree of restlessness is to be expected, and bodily movements per se, should not be regarded as abnormal. If considerable cerebral irritation is evident, intravenous magnesium sulfate should be repeated as necessary, but in this as in the first stage all sedation is limited.

The continued use of intravenous hypertonic dextrose solutions may be necessary early in this period, but as a rule fluids can be given orally, especially if sedation is limited. In the eclamptic woman, just as in normal individuals, a larger urinary output is stimulated by oral than by parenteral fluids. As soon as the swallowing reflex has returned, a minimum of 200 c.c. of highly sweetened fruit juice is given each hour, it being the duty of the nurse or physician to administer it as regularly as if it were a prescribed medication. Water, coca cola, milk, coffee, tea or beer may be taken as desired. Many patients will take several times the minimum required amount of fluid, and should be encouraged to take as much as they comfortably can, though fluids should not be

pushed to the point of nausea. Copious diuresis and clinical improvement are frequently observed a few hours after the oral intake of fluids is begun, even in patients whose response to parenteral dextrose therapy has not been satisfactory.

The Management of the Controlled-Eclamptic Stage

Toward the end of the postconvulsive and in the first part of the controlled-eclamptic stages, the patient, if the response to treatment has been satisfactory, may be drowsy but she can be roused and she is usually fairly well oriented. Very little sedation is required, and she is taking large quantities of fluids by mouth. The gastrointestinal tract is clean. The blood pressure is stabilized in the range between 150 and 170 systolic, and the pulse pressure is approximately normal. Edema disappears slowly. The urinary output, even though diuresis may not be free, maintains a safe relationship to the intake. Proteinuria gradually disappears, at first slowly and then at a more rapid rate. Serial cell volume determinations reveal progressive improvement in hemoconcentration.

There is considerable variation in the rapidity and extent of improvement in the controlled-eclamptic stage. Residual mild headache and visual disturbances may be present early in this stage, but more often the only notable abnormality is some degree of lethargy. Improvement, though usually gradual, is noticeable from day to day, and 4 to 10 days after the attack, the patient's status suggests a mild pre-eclampsia. Some subjects, indeed, would be considered normal if the history of convulsions were withheld. Sometimes spectacular improvement is seen immediately subsequent to the convulsions and coma, and even when the improvement is gradual many patients are so well that it is difficult to keep them in the hospital.

The therapeutic regimen during the controlled-eclamptic stage is as follows:

1. *Continued Hospitalization and Observation.*—It is imperative that the eclamptic patient remain in the hospital following control of her seizures, and that she remain in bed, though she may move about at will, and may have a back rest.

Continued constant observation during this period is essential. An experienced obstetrician visits the patient at least twice daily, taking time during each visit to review the regular hospital chart and the special toxemia record, and to elicit from the patient herself even apparently minor symptoms. In his absence she is under the continuous observation of a trained nursing and resident staff, the members of which are fully aware of the possibility of adverse changes and of how they will manifest themselves.

2. *Special Diagnostic, Prognostic and Other Examinations.*—Special examinations, which are most conveniently recorded on a special toxemia sheet, include:

Blood pressure determinations at four-hour intervals when the patient is awake, unless there are indications for more frequent determinations.

Accurate volumetric determinations of the daily fluid intake and daily urinary output, which are recorded at eight-hour intervals, since oliguria or anuria may develop rapidly. The patient is weighed daily and the body weight and urinary output are roughly correlated, to estimate the water balance of the body.

Daily qualitative and quantitative determinations of urinary albumin. A sample of the 24-hour volume of urine is used for this purpose.

Microscopic examination of the sediment of a catheterized specimen of urine at intervals of several days.

A daily hematocrit, to determine tendencies toward hemoconcentration or hemodilution. It should be emphasized, in this connection, that because of hemoconcentration hypoproteinemia, with or without anemia, may be overlooked.

Ophthalmoscopic examination as soon as the patient can be disturbed. This examination is repeated at frequent intervals, as changes in the retina often precede changes elsewhere in the body.

Certain special examinations and tests, such as tests of renal and hepatic function, and determinations of venous pressure, circulation time, vital capacity, vascular lability and blood chemical values, as well as electrocardiography, are all interesting, but on the whole, as we have practiced them, they have not supplied consistent or conclusive information. Serial blood chemical determinations, especially of the carbon-dioxide combining power of the blood, the uric acid of the blood and the serum protein concentration may be of prognostic value, but on the whole, are of so little help from any standpoint, that lack of facilities for their determination cannot be accepted as a valid excuse for inadequate treatment of, or poor results in, eclampsia.

3. *Therapeutic Measures.*—Fluids are given entirely by mouth unless some special indication for parenteral dextrose therapy arises. The daily fluid intake is maintained at 4,000 c.c. or over, but patients frequently take much larger quantities without urging, and outputs of 6 to 8 liters per day are correspondingly frequent. A high-protein, salt-free diet is prescribed, which contains 2,000 calories per day and provides approximately 100 Gm. of protein. Supplementary vitamins and minerals are also prescribed.

A saline cathartic is given every third morning. Ammonium chloride in doses of 1 Gm., four times daily, is sometimes helpful if diuresis is not entirely satisfactory. Sodium phenobarbital in doses of 1.5 to 3 gr. is given by mouth to insure sufficient rest at night, but in the absence of indications is withheld during the day. Other hypnotics are avoided, for oversedated patients frequently become irritable and even disoriented, and may complain of headache, nausea and visual disturbances.

4. *Termination of Gestation at the Optimum Time and by the Simplest Possible Method.*—Radical treatment, in which the child is forcibly delivered in the hope of stopping the convulsions, is now universally condemned. On the other hand, it is still common practice, as soon as convulsions are apparently controlled, to induce labor by irritating if not actually traumatic procedures, and to resort to abdominal section if these methods are not promptly successful. This unphysiologic practice, in our opinion, is responsible in no small measure for a definite number of maternal and fetal deaths.

It is to the advantage of both mother and child to defer the termination of pregnancy for a period of time after eclampsia is definitely controlled. From the standpoint of the mother, delay permits the induction of labor with minimum trauma, by progressive gentle stimulation which

results in a normal mechanism of labor, whereas fatalities are not uncommon when induction by bag, bougie or packing is carried out or when cesarean section is performed on a toxic subject. Furthermore, labor often begins spontaneously during the waiting period.

From the standpoint of the child, its chances, like the mother's, are better if recovery from the acutely toxic maternal state is permitted, as well as recovery from the effects of sedation by which that state was controlled. Traumatic procedures, whether for induction of labor or for the purpose of delivery, affect the child adversely. Finally, the nearer the premature child approaches maturity, the better are its chances of life, even though the delay may seem insignificant. The danger of intra-uterine fetal death during the period of convalescence has been exaggerated. In this series there were only three such deaths, on the second, third and sixth days following the convulsions. It is possible that these children would not have survived under any circumstances, since their weights varied from 4 pounds, 12 ounces to 3 pounds.

The arguments against the policy of delay are readily answered. It is quite true that even under the most careful regimen there is always danger of sudden recurrence of fulminating toxemic manifestations or of actual convulsions, but this is not frequent. In our own series eclampsia did not recur in a single instance during the waiting period, and in only two cases were signs of their impending return sufficiently serious to demand immediate emptying of the uterus by cesarean section; medical induction had failed in one of these cases.

The danger of permanent damage to the vasculorenal and other systems as the result of delay is also not great. In our own cases, in fact, clinical and laboratory observations revealed such marked improvement, which in some instances amounted to a return to normal status, that we are unable to conceive of the delay as a basis of residual pathology. Furthermore, the incidence of residua found at the follow-up of these patients was no greater in the antepartum than in the other groups. It should be emphasized that this statement covers the group of patients who were delivered more than seven days after the onset of their convulsions, which seems to make clear that intercurrent

TABLE IV. TIME INTERVAL FROM THE FIRST CONVULSION TO DELIVERY

TIME INTERVAL	NUMBER OF CASES	PER CENT
<i>Antepartum Eclampsia</i>		
Less than 24 hours	6	8.1
24 to 72 hours	17	22.8
3 to 7 days	26	35.3
More than 7 days	25	33.8
Average 6.7 days	74	100.0
<i>Intrapartum Eclampsia</i>		
Less than 6 hours	10	33.3
6 to 12 hours	10	33.3
12 to 24 hours	7	23.4
More than 24 hours	3	10.0
Average 7.7 hours	30	100.0
<i>Postpartum Eclampsia</i>		
Less than 1 hour	5	13.2
1 to 6 hours	11	28.9
6 to 12 hours	10	26.3
12 to 24 hours	7	18.4
More than 24 hours	5	13.2
Average 8.5 hours	38	100.0

eclampsia need carry no higher a mortality and no higher an incidence of residua than any other variety.

The longest interval in our series between the onset of convulsions and delivery was 38 days (Table IV). The patient, a 21-year-old primipara, had had seven typical eclamptic convulsions, accompanied by severe hypertension and massive edema; the urine boiled solid. A mild toxemia evident at delivery disappeared within 10 days, and at the last examination, seven months later, there was no trace of any abnormality. Her child, who weighed 3 pounds and 9 ounces at delivery, then weighed 18 pounds.

The added expense of continued hospitalization, the constant care and supervision required, and the anxiety of the patient and her family are not valid reasons for prompt delivery when weighed against possible maternal and fetal salvage, inherent in the more conservative policy.

The policy of watchful expectancy in this series resulted in the spontaneous onset of labor in 42 of the 74 cases of antepartum eclampsia (Table V), the interval from the final convulsion to the onset of labor varying from three hours to 37 days.

If the patient is in good condition and close to term, there is, of course, no contraindication to the prompt induction of labor, which should also be carried out without delay in patients who do not show a satisfactory response to therapy, or who present a relapse which is not promptly controlled. This occurred in 10 cases in this series, though in no instance was it necessary to terminate pregnancy by cesarean section without first attempting induction of labor.

Even under the best of circumstances, however, we do not favor postponing induction indefinitely if labor does not set in spontaneously, for medical induction is not infallible but rather a slow process, often requiring several repetitions of the stimuli, and hurried interference would be undesirable if adverse changes should suddenly occur. Fortunately, toxemia seems to increase the irritability of the uterus, as evidenced not only by the 57 per cent of antepartum cases in this series in which labor occurred spontaneously, but also by the fact that an additional 5 per cent responded to the first attempt at medical induction.

TABLE V. TIME INTERVAL FROM THE FINAL CONVULSION TO THE SPONTANEOUS ONSET OR ATTEMPTED INDUCTION OF LABOR IN 74 CASES OF ANTEPARTUM ECLAMPSIA

TIME INTERVAL	NUMBER OF CASES			TOTAL CASES
	HAVING SPONTANEOUS ONSET OF LABOR	HAVING INDUCTION OF LABOR		
		ELECTIVE	REQUIRED	
Less than 12 hours	8			8
12 to 24 hours	3		2	5
24 to 48 hours	1		1	2
48 to 72 hours	9	1	2	12
3 to 5 days	4	8	3	15
5 to 7 days	6	5	1	12
7 to 10 days	6	3		9
10 to 15 days	2	3	1	6
More than 15 days	3	2		5
	16 days	17 days		
	19 days	19 days		
	37 days			
Total cases	42 (57%)	22 (30%)	10 (13%)	74
Average interval	5.6 days	5.1 days	3.9 days	5.2 days

The simplest method of medical induction is as follows: At 6 A.M. the patient is given 1.5 ounce of magnesium sulfate by mouth, and at 10 A.M. a high hot soapsuds enema is given. At 2 P.M., if no contractions have occurred, 0.5 minim of pitocin is injected subcutaneously. The injection is repeated every 20 minutes, in an amount 0.5 minim greater than the preceding dose, until rhythmic contractions ensue or until a maximum dosage of 3 minims has been obtained. The attempt is repeated every 24 or 48 hours in cases in which the first induction fails, for each attempt, even though unsuccessful, seems to soften and shorten the cervix and to increase uterine irritability until labor finally sets in. We have never observed a serious reaction when pitocin has been used within the limits defined by an experienced obstetrician.

Induction was successful in 16 of the 32 cases in which it was carried out in this series, although 3 patients required 2 inductions, 5 required 3, 2 required 4, and 2 required 5 attempts each. Success was attained within 24 hours in 18 per cent of these cases, within 48 hours in 34 per cent, and within 72 hours in 65 per cent.

When simple measures fail and greater haste seems indicated, as happened in 11 cases in this series, the vagina is liberally cleansed with green soap, after which the cervix is slowly and carefully stretched until it admits at least one finger. The membranes are then stripped from the lower uterine segment. If contractions do not occur within two hours, a course of pitocin is begun. In 4 cases, rupture of the membranes was necessary; in another instance, labor was terminated by cesarean section, because of the presence of a long, firm, closed cervix in a nullipara.

TABLE VI. LENGTH OF LABOR

	TYPE OF ECLAMPSIA			PER CENT OF TOTAL CASES
	NUMBER OF CASES			
	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	
Less than 4 hours	16		4	15.0
4 to 8 hours	25	2	18	33.7
8 to 12 hours	9	9	5	17.3
12 to 16 hours	8	5	4	12.8
16 to 24 hours	10	5	3	13.6
More than 24 hours	3	4	3	7.5
Delivered by section	3	5	1	6.3
Total cases	74	30	38	
Average time	5.5 hours	13.4 hours	8.6 hours	7.9 hours

The Management of Parturition

Labor was of surprisingly brief duration in most of the 133 patients in the series who were delivered vaginally; the range was from 0.5 to 41.7 hours, but the average was 7.9 hours (Table VI). The longest labors were observed in the intrapartum group, possibly because of the depressing effects of sedation early in labor.

Operative methods of delivery were held to a minimum in order to obviate the ill effects of unnecessary trauma, anesthesia, blood loss and infection in these highly susceptible patients. One hundred nine patients, 76.8 per cent of the total number, accomplished natural spontaneous delivery; the lowest incidence of operative delivery, 16.2 per

cent, was in the antepartum group (Table VII). The chief indication for operative vaginal delivery was prolongation of the second stage of labor, with possible jeopardy to both mother and child.

TABLE VII. METHOD OF DELIVERY

	TYPE OF ECLAMPSIA			PER CENT OF TOTAL CASES
	NUMBER OF CASES			
	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	
Vaginal Delivery	71	25	37	93.7
Spontaneous	62	18	29	76.8
Forceps	5	4	6	
Breech extraction	2	2	1	
Version and extraction	1		1	
Embryotomy	1	1		
Abdominal Delivery	3	5	1	6.3
Cesarean section	3	3	1	
Cesarean section plus hysterectomy		2		
Total	74	30	38	100.0

Cesarean section was performed only nine times, 6.3 per cent, and eclampsia per se was the indication for section in only four of these patients. Dystocia furnished the indication in two cases, and placenta previa, abruptio placentae, and infection plus dystocia in one case each. Cesarean section was followed by hysterectomy in the last two cases mentioned. Abdominal delivery was performed only once in the 51 cases handled in the last two years, in the patient who required the Porro operation for infection and dystocia, and the declining incidence of section is an interesting commentary on our increasing tendency to treat the disease rather than the pregnancy.

Local analgesia was used for all varieties of operative work. We consider all other forms of anesthesia dangerous in eclampsia, and have made no exception of caudal techniques since we observed a patient with pre-eclampsia develop convulsions five hours after delivery under continuous caudal analgesia.

Although labor is short and delivery easy in most cases of eclampsia, constant watchfulness must be maintained, for the ordinary hazards of parturition are always increased. Irritation and trauma, whether endogenous or exogenous, may precipitate convulsions and make control increasingly difficult. Restlessness may make sedation necessary. The low urinary output frequently encountered late in labor may call for special therapeutic measures. The abrupt development of such complications as pulmonary edema and vascular collapse may tax one's ingenuity to the uttermost.

Obstetric complications, furthermore, are not uncommon, and their management is difficult because these patients do not tolerate even ordinary manipulations and ordinary blood loss. It is not always easy to determine whether the conditions encountered are due to eclampsia, to normal or abnormal circumstances of parturition, to the therapeutic

measures adopted for the control of eclampsia, or to the cumulative effect of all these factors. Eclampsia is the basic disease, it is true, but the obstetric complications cannot be disregarded.

The complications which occurred in this series involved 21 per cent of the patients. They included hemorrhagic complications in 13 cases (abruptio placentae in 7 cases, postpartum hemorrhage in 4, and placenta previa in 2), vascular collapse in 3 cases, polyhydramnios, serious dystocia and severe intrapartum infection in 2 cases each. Eight cases had severe anemia.

The Management of the Puerperium

The rather general belief that the successful termination of labor is equivalent to the successful termination of the eclamptic state is by no means justified. It is true that in no case in our series did convulsions recur after delivery, and that in most instances definite amelioration of toxic manifestations occurred within 24 hours of delivery; even cases of intercurrent eclampsia usually responded with increased diuresis during this period. On the other hand, in the 104 cases of antepartum and intrapartum eclampsia in this series, there were at this time three instances of peripheral vascular collapse, and four instances each of postpartum hemorrhage, persistent anuria, and profound coma.

Convulsions and serious complications not infrequently develop following delivery, certain precautions, in addition to routine postpartum measures, are necessary during the puerperium and, in particular, immediately after delivery. An intravenous infusion of 20 per cent dextrose solution in the amount of 500 c.c. is begun as soon as the patient is prepared for delivery, and is administered very slowly. This measure aids in the prevention of shock and collapse when the child is born, and obviates the difficulty of entrance into veins if vascular collapse should occur. Morphine is administered as soon as delivery is completed.

The blood pressure and urinary output are checked regularly throughout the period of hospitalization, and mother and child are kept in the hospital for a minimum of 10 days and preferably for 14 days. Although 50 per cent of postpartum convulsions occur within 8 hours of delivery, they can begin much later (41 hours in this series), and prolonged observation of potentially eclamptic patients is imperative.

The patient then returns at regular intervals to the postpartum clinic, and it is impressed upon her that she should submit herself to examination at regular intervals throughout the remainder of her life, especially if she again becomes pregnant.

Results of Therapy

Maternal Results.—The fact that there were no maternal deaths in these 142 cases of eclampsia, we attribute to our strict adherence to

the plan of treatment just outlined. On the other hand, we were not asked in this series to accomplish the impossible. Patients transported from distant areas did not succumb before treatment could be administered, and we encountered no cases of such uncommon but apparently invariably fatal complications as acute heart failure, extensive cerebral hemorrhage, or massive pulmonary edema of degrees incompatible with life.

From the standpoint of morbidity, we were less successful, for, by accepted standards, it averaged 36.6 per cent, which is more than four times greater than the incidence in our usual obstetric census. The rate was highest in the postpartum group (57.8 per cent) and lower by 40 per cent (22.9 per cent) in the antepartum group, most of the patients in which had recovered from the acute phase of the disease. It was 43.3 per cent in the intrapartum group. Hyperpyrexia, with temperatures above 104° F. during the convulsive or comatose stages, occurred in four cases, probably as the result of temporary derangement of the temperature centers by vasospasm or edema. Other common extragenital causes of fever were pulmonary congestion and edema, urinary tract infections, and reactions to parenteral fluids or to sedation.

Seventy-eight per cent (26) of the 33 patients delivered by operative means had febrile puerperia, and this increased susceptibility should serve as a warning to limit intervention in eclampsia to cases in which the indications are indubitable.

Fetal Results.—Of the 149 children born to the 142 mothers in this series, 113, 75.8 per cent, were discharged from the hospital in satisfactory condition. Although the fetal case fatality was 24.2 per cent (36), the salvage from the seven twin pregnancies fortunately permitted 111 women to leave the hospital with children.

Previability and prematurity were responsible for 31 of the 36 fetal deaths (86.1 per cent). Among the 5 mature infants who failed to survive, premature separation of the placenta was the cause of 1 death and intrapartum uterine infection of another, but in the other 3 cases no definite cause was found. Twenty-two babies were stillborn, several of whom were dead when the mother was admitted to the hospital. Necropsies were done in 25 cases, in 16 of which (64 per cent) varying degrees of intracranial hemorrhage were found.

Birth weights (Table VIII), which were invariably less than the clinic average for similar stages of pregnancy, showed the direct effect of toxemia upon the fetal growth and development, as well as the effect of prematurity. Fourteen babies (10 per cent) weighed less than 1,500 Gm., and were classed as previable; 62 others (42 per cent) weighed between 1,500 and 2,500 Gm., and were classed as premature. Most of the remaining 73 children, despite the increased gestation period and increased birth weight, appeared toxic and immature. The proportion of survivors, however, almost consistently increased in direct ratio to increases in the birth weights.

Twenty-four of the 36 deaths occurred in the antepartum group (32.4 per cent), 8 in the intrapartum group (26.6 per cent), and 4 in the postpartum group (10.5 per cent). The lowest fetal case fatality would naturally be expected in the group which escapes the shock of convulsions and is least affected by prematurity, and the highest would be expected in the group affected by the combination of prematurity and convulsions. The fetal mortality in severe eclampsia was 36 per cent, as compared with 23 per cent in mild eclampsia.

TABLE VIII. FETAL DEATHS IN RELATION TO FETAL BIRTH WEIGHTS

BIRTH WEIGHT	TOTAL CASES	DIED		SURVIVED	
		STILL-BORN	NEONATAL	NUMBER	PER CENT
Under 1,000 Gm.	4	3	1		
1,000 to 1,499 Gm.	10	5	3	2	20.0
1,500 to 1,999 Gm.	25	8	5	12	48.0
2,000 to 2,499 Gm.	37	3	3	31	83.8
2,500 to 3,499 Gm.	65	3	1	61	93.8
3,500 Gm. and over	8		1	7	87.5
Total	149	22	14	113	75.8

Incidence of mortality—24.2 per cent

Average weight of all babies-----2,660 Gm.

26% of all babies weighed less than-----2,000 Gm.

67% of all dead babies weighed less than-----2,000 Gm.

64% of all babies under 2,000 Gm., died.

Although the fetal case fatality in this series compares favorably with that in other reports in the literature, in retrospect we consider it unnecessarily high. In the early years of this study we believed a high fetal mortality inevitable in eclampsia, and we hesitated to do anything for the sake of an infant whose existence seemed precarious at best, lest we jeopardize the mother's safety. In later years, we have found that reasonable attention to the baby yields high dividends. We have not changed our basic plan of treatment in any way for the child's sake, but in the last two years of this study, with the close cooperation of the Department of Pediatrics, we have achieved a gross fetal mortality of 17.6 per cent in 51 cases. Undoubtedly, this rate can be still further improved by proper attention to the child before, during, and after delivery.

Follow-Up

Seventy-two patients, more than 50 per cent, were normal in all respects on their discharge from the hospital from 5 to 31 days after delivery, and it is significant that no woman in this group later exhibited hypertension. In two instances, complete amaurosis had returned to normal by this time.

The remaining 70 patients presented blood pressure elevations of 140/90 or higher when they were dismissed from the hospital after delivery, and 11 of these presented associated albuminuria. It is significant that the elevations of blood pressure occurred in only 36 per cent (9) of the 25 patients with intercurrent eclampsia of more than seven days' duration, as compared with 32 of the 49 patients who had been delivered within 7 days after their seizures (65 per cent), and 41 of the 74 patients who comprised the whole group of patients with antepartum eclampsia (55 per cent).

Elevated pressures were also observed in 19 of the 30 patients with intrapartum eclampsia (63 per cent) and in 10 of the 38 patients with postpartum eclampsia (26 per cent).

Eighty-five of the 142 patients were observed in the clinic at periods varying from 5 to 12 weeks after delivery. Seventy-three were then normal in all respects (42 of 49 in the antepartum group, 15 of 18 in the intrapartum group, 16 of 18 of the postpartum group). The re-

maining patients had elevations of blood pressure above 140/90. Again it is significant that only 2 of the 18 patients in the intercurrent group presented elevated pressures, as compared with 5 of the 31 patients in the antepartum group who had been delivered within 7 days.

Forty-six of the 142 patients were again observed at periods varying from 1 to five years after their attacks of eclampsia. All these patients were admitted to the hospital, where investigation included complete physical examination, urinalysis, blood chemical determinations, urea clearance tests, tests of hepatic function, electrocardiographic studies, and studies of vasomotor lability. The only abnormalities apparent in any of these tests were persistently elevated blood pressures, varying from 140/90 to 170/110, in 3 patients, who were regarded as having hypertensive vascular disease. Again, it seems significant that only one of the 11 patients re-examined in the intercurrent group exhibited this abnormality, as compared with 1 of the 15 re-examined in the group delivered within 7 days of their seizure, and 1 of the 12 re-examined in the intrapartum group. No elevated pressures were observed in the 8 patients with postpartum eclampsia who were re-examined.

The number of patients re-examined is small and the period of observation somewhat limited, but the results to date do not suggest that eclampsia, regardless of its type, severity or duration, causes permanent vascular or renal damage or any other sequelae.

Thirty-four of the 142 patients have been followed in 56 subsequent pregnancies. Eleven women had 2 pregnancies each, 4 had 3 pregnancies each, and 1 had 4 pregnancies within the five-year period of observation. Forty-six of these pregnancies in 26 patients (76.4 per cent of the group followed-up) were normal in all respects, including the 4 pregnancies in the five-year period.

The remaining 8 patients, however, who went through 10 subsequent pregnancies, all exhibited some form of toxemia at some time. One patient had a recurrence of eclampsia, the conditions in both pregnancies being identical: After more than average prenatal care, mild pre-eclampsia developed and culminated abruptly in convulsions during labor. One patient developed mild pre-eclampsia in the first subsequent pregnancy and severe pre-eclampsia in the second, the blood pressure and urine being normal in the interims. It would seem advisable to terminate childbearing in both these women, as well as in 2 other women who were found to have persistent hypertension in the second and the third pregnancy, respectively, after the pregnancies in which eclampsia developed. Three other women had mild pre-eclampsia in one successive pregnancy each, and the remaining patient had the same condition in two successive pregnancies; it would seem best either to sterilize this latter patient, or to advise the use of contraceptive measures until her true status can be determined.

Although the incidence of toxemia in the posteclamptic group is approximately double the clinic average, it is doubtful whether eclampsia should be regarded as the only cause of the increase. If comparison were made with a group of women subjected to the similar stress and strain of repeated pregnancies in rapid succession, but without a history of eclampsia, the incidence would probably be much the same. On the other hand, the high rate of fecundity warrants consideration, for it undoubtedly accelerates, or at least aggravates, the development of potential, incipient, or active vascular or renal disease. Eclampsia

by no means precludes the possibility of subsequent normal pregnancy, but childspacing is advisable, and medical care in subsequent pregnancies is imperative.

Prophylaxis

Reports in the literature are unanimous in emphasizing the value of prenatal care in the prophylaxis of eclampsia, and the lack of such care was the obvious cause of the development of most cases in this series (Table IX). In 91 cases, almost 65 per cent of the total, the patients had no care of any kind during their pregnancies, and in another 37 cases such care as they had was entirely inadequate by modern obstetric standards.

It might be interpolated here that the financial status and intelligence ratings of these women compared favorably with the general average in such material.

Eclampsia developed in only 14 patients who attended the clinic regularly throughout pregnancy, and at first glance all of them seemed to have received excellent prenatal care. Closer investigation, however, usually revealed lack of full cooperation on their part, or errors of judgment on the part of the physician, in sharp contrast to modern concepts of adequate and intelligent prenatal supervision. Curiously, defections, most of which occurred late in pregnancy, were explained in the same way in almost all cases; the patients were "too sick to come to clinic" or "too sick to do what the doctor said."

Even under the best of circumstances eclampsia is not entirely preventable. Occasionally, a rapidly fulminating pre-eclamptic toxemia culminates in convulsions without the usual, gradually progressive phases, and still more occasionally all antecedent manifestations are absent. Three of our cases were in the latter category. The patients were apparently normal in all respects throughout their pregnancies, and had received competent medical attention in the prenatal clinic, 6, 14 and 21 hours, respectively, prior to the onset of convulsions. One patient complained of a mild antecedent headache, but in the other two cases, so far as could be determined, there were no premonitory symptoms or signs of any sort.

TABLE IX. PREVENTION AND RESPONSIBILITY IN RELATION TO THE TYPES OF ECLAMPSIA

TYPE OF ECLAMPSIA	PRENATAL CARE			ONSET OF CONVULSIONS		
	ADEQUATE	INADE- QUATE	NONE	AT HOME	IN HOSPITAL	EN ROUTE TO HOSPITAL
Antepartum	8	20	46	47	15	12
Intrapartum	4	12	14	11	16	3
Postpartum	2	5	31	10	26	2
Total	14	37	91	68	57	17
Per cent	9.9	26	64.1	48	40.1	11.9

NOTE: A detailed case report is appended, which may clarify the plan of management in a typical case.

RÉSUMÉ OF CLINICAL COURSE AND TREATMENT IN A TYPICAL CASE (HOSPITAL NO. L-42-69985) OF ANTEPARTUM ECLAMPSIA IN AN 18-YEAR-OLD COLORED NULLIPARA WHO HAD NO PRENATAL CARE

DATE	BLOOD PRES-SURE	URINE		EDEMA	BLOOD CHEMISTRY	CLINICAL CONDITION	TREATMENT
		C.C.	ALBUMIN				
11/9/42	190/120			+++	Hematocrit* 55.0 Uric acid† 6.9 Serum protein‡ 5.8	5 convulsions before admission, 1 on admission	2:45 P.M. Morphine sulfate, $\frac{1}{4}$ gr. } subcuta- Sodium phenobarbital, 5 gr. } neously
3:00 P.M.	170/110	20 (casts)	Boiled solid	Lungs - + Face + +			3:00 P.M. Retention catheter
3:30 P.M.	175/110					Restless, spastic	3:30 P.M. Magnesium sulfate (10%) 20 c.c. intravenously
4:00 P.M.	180/110	12					4:05 P.M. Nasal oxygen
6:00 P.M.	160/110	25					Glucose (20%) 500 c.c. intravenously
8:00 P.M.	160/115	65	+++			Semicomatose	6:00 P.M. Phenobarbital, 5 gr. subcutaneously
10:00 P.M.	165/115	15				Irrational	10:00 P.M. Glucose (10%) 1,000 c.c. intravenously
12:00 M.	160/100	185	++	+++	Hematocrit 50.0	Vomiting T. 103.2 F.; P. 120; R. 40	12:00 M. Magnesium sulfate (10%) 20 c.c. intravenously
11/10/42	180/112					Semicomatose Stuporous, irritable	2:15 A.M. Glucose (50%) 50 c.c. intravenously
3:30 A.M.	162/105	455					3:30 A.M. Phenobarbital, 5 gr. subcutaneously
8:00 A.M.	170/120	280	++	++		Restless Conscious, drowsy	8:00 A.M. Phenobarbital, 5 gr. subcutaneously
12:00 M.	160/100	20			Hematocrit 42.0 Uric acid 4.9 Serum protein 5.2	Retinal vasospasm and edema	12:00 M. Glucose (20%) 500 c.c. intravenously Force fluids orally
4:30 P.M.	155/110	300					4:30 P.M. Magnesium sulfate orally
8:00 P.M.	175/115	590	++	+		Headache T. 99 F.; P. 100; R. 22	8:00 P.M. Enema
12:00 N.	145/100	725					24-hour fluid intake—3,780 c.c.

*In cell volume per cent.

†In mg. per cent.

‡In Gm. per cent.

11/11/42 8:00 A.M. 4:00 P.M.	140/100 148/105	No casts	++ +	++ Lungs— negative	Hematocrit 36.0 Serum protein 5.7	Rational Sleeping, quiet T. 97.8; P. 84; R. 20	Diet: protein 100 Gm., salt free Fluids: forced to 5,000 c.c. orally Sedation: phenobarbital orally, P.R.N. Elimination: magnesium sulfate orally
12:00 M.	155/105	4485	+				Intake—5,100 c.c.
11/12/42	155/115	3535	0	+		Mild headache	Intake—3,950 c.c.
11/13/42	144/100	4260	+	+		Cooperative	Intake—5,700 c.c.
11/15/42	150/110	4900	++	Ankles	Hematocrit 36.1	No complaints	Intake—4,080 c.c.
11/18/42	140/90	3690	0	0		No complaints	Intake—4,330 c.c.
11/20/42	150/90	3745	0	0			Medical induction, membranes stripped
11/21/42 A.M. P.M.	168/100 140/100	920 485	++ +	0 0		Labor—13 hours Baby—alive; wt. 6.1 pounds	Labor: Morphine, gr. $\frac{1}{4}$; glucose (20%) 500 c.c. Delivery: low forceps, episiotomy; local analgesia. Morphine and glucose infusion during delivery
11/22/42 11/29/42	140/90 135/85	3160	Tr. 0	0 0	Hemoglobin† 10.0 Hematocrit 32.5 Serum protein 6.2	Mother and baby in good condition	Discharged from hospital
1/ 6/43	120/80	Sediment negative	0	0		Same	
12/14/43	108/65	Sediment negative	0	0	Hemoglobin 11.1 Uric acid 3.8 Serum protein 7.5	Mother and baby in excellent condition	Electrocardiogram—negative Ocular fundi—negative
3/22/44	110/78						Electroencephalogram—normal

Seventeen patients had their first seizures while en route to the hospital (Table IX) and 57 others after being admitted to the hospital. Most of these women sought aid because of fulminating symptoms, such as severe headache, drowsiness, dim vision, vomiting, or marked edema, but 5 other patients came merely because they "felt funny" and evidently had premonitions of danger.

A review of the cases in which the first convulsions occurred after hospitalization shows that in at least 34, adequate attention, sufficient sedation, the use of hypertonic dextrose solution, and the induction of labor might have prevented the convulsions. These cases all represent failures of management, though the human factor could not always be held responsible. In the remaining 23 cases, the seizures occurred within two hours of hospitalization and could scarcely have been prevented.

These 142 cases bear witness to another precaution quite as important as prenatal care but less often emphasized, namely, that intelligent care and good judgment are as essential during labor and after delivery as during the antenatal period. In this series 68 patients, 47.9 per cent, had intrapartum or postpartum convulsions, and it is reasonable to speculate that if parturition and the early puerperium had been managed with more attention to possible dangers, some if not all of these seizures might have been prevented.

Summary and Conclusions

1. There is presented in this paper a plan of management of eclampsia as the result of which no maternal deaths occurred in 142 personally supervised cases. So far as can be determined, this is the largest successful series to be recorded.

2. The therapeutic regimen outlined is neither new nor original, but it is believed that the details of its application are not always carried out with the care with which they were applied in this series. To that unremitting care are attributed the successes which were achieved.

3. The plan is based on (a) an ultraconservative concept of management, in which the dangers of both overtreatment and indiscriminate treatment are evaluated; (b) constant (in the most literal sense of the word) observation of each eclamptic patient by an experienced staff throughout the entire course of treatment, which permits (c) careful integration of the various therapeutic components into an individualized regimen rather than their application as a standard routine of treatment.

4. Special factors of success also include: (a) frequent changes of posture, plus the use of oxygen therapy and of aspiration, during the acute phases of the disease; (b) limitation of sedation to the dosage necessary to control convulsions and hyperirritability; (c) limitation of dextrose therapy to the smallest amount necessary to insure a satisfactory urinary output, with a return to oral fluids in maximum amount as soon as the swallowing reflex returns; (d) delaying labor

(unless it ensues spontaneously) until the optimum recovery from the acute stage has taken place; (e) induction of labor at the optimum time and by the simplest possible method, medical induction being repeated if the first attempts are not successful; (f) limitation of operative intervention to the irreducible minimum, and the use of local analgesia for all forms of operative work.

5. Neither the patients' future health nor their subsequent pregnancies are in any way jeopardized by this plan of management. This statement is based upon (a) observation of 85 patients at intervals of from 5 to 12 weeks after delivery; (b) of 46 patients at intervals of from 1 to 5 years after delivery; (c) and of 34 patients in 56 subsequent pregnancies. The incidence of residua was no larger in the intercurrent group of patients than in the whole group followed up and was smaller than in some of the subgroups.

6. Adequate consideration of the baby yields high dividends in fetal salvage without increasing the maternal risk. The fetal case fatality in this series was 24.2 per cent; it showed marked improvement in the last two years, when the principle of consideration for the child was increasingly applied.

7. Lack of adequate prophylaxis was the factor chiefly responsible for the development of eclampsia in these 142 cases. In this respect, adequate care during gestation is not sufficient. Intelligent care and sound judgment are also needed during labor, at delivery, and throughout the puerperium.

Discussion in the Papers by Drs. Huber and Arnell

DR. CHARLES H. PECKHAM, Cooperstown, N. Y.—Dr. Arnell is to be congratulated on such a lengthy series of cases without a maternal death, but I am afraid my own experience more closely parallels that of Dr. Huber.

Since the incidences of and mortality from eclampsia apparently vary greatly in different localities of this country, as well as in different parts of the world, attempts to adduce conclusions from comparative statistics are open to a good deal of criticism. The transition from so-called radical to conservative therapy began about thirty years ago, and the latter has been the rule in most clinics in this country for about twenty years. Conservative regimes of treatment at present differ essentially only in the type of sedative drugs employed. Morphine, magnesium sulfate, sodium luminal, sodium amytal, chloral hydrate and paraldehyde have probably been employed most frequently. Since the main object of drug therapy is the prompt control of the convulsive seizures, it is interesting to speculate why one drug works better for one clinician and a different one for another. The answer is probably very simple—none is completely satisfactory.

It is a matter of rather general agreement that present therapy gives satisfactory results in cases of eclampsia classified as mild, but leaves a great deal to be desired in the severe type. A number of years ago, I analyzed the records of 152 cases of convulsive toxemia of pregnancy divided into mild and severe groups according to a proposed modified Eden type of classification. No maternal deaths occurred in 71 cases denoted as mild, while in 81 instances of severe eclampsia the mortality was 18.5 per cent. It was also noted that as conservative treatment replaced radical, the mortality from antepartum eclampsia fell to one-half of that formerly observed, intrapartum to one-quarter, while the results in

the postpartum type were unchanged. As a matter of fact, postpartum eclampsia in my experience as opposed to that of many others, carries a higher mortality rate than that of the other types.

The death rate from eclampsia has furthermore shown a general tendency to decline during the past ten years. Is this due to improved treatment or a decline in severity of the disease? Some time ago an article appeared in the literature demonstrating a lower mortality from eclampsia coincident with certain alterations in therapeutics; during the same time interval, a similar decrease was noted at the Johns Hopkins Hospital although therapy was unchanged. Most authorities attest to a lowered incidence of eclampsia itself. Is this due to a generally improved prenatal regime, to better treatment of the patient with early toxemia, or to an increased tendency to terminate the pregnancy immediately if severe pre-eclampsia manifests itself? All of these three probably play a role, but the prophylactic emptying of the uterus by whatever means seems best has not yet received the popularity it deserves.

Dr. Arnell's remarks concerning the treatment of the early toxemic patient cannot be too strongly emphasized. The importance of proper elimination and the prohibition of salt in the diet is generally agreed upon. On the other hand, we have only begun to realize the importance of the protein problem. Fifteen years ago patients with toxemia of pregnancy were placed upon low protein diets and seemed to improve. Why? One wonders if the type of protein previously ingested supplies at least a partial answer. The diet of the average ward patient is frequently deficient in milk, eggs, and cheese, and the principal source of protein is often ham and pork. Gastroenterologists agree that pork and veal are by far the most difficult meats to be assimilated by digestive processes. If it is agreed that the toxemic patient requires in the neighborhood of 100 grams of protein per day, these can safely be supplied by a quart of milk, two eggs, the usual fruits and vegetables, one serving of cheese and one of meat.

I question the wisdom of allowing the patient with a live fetus to proceed indefinitely with her pregnancy subsequent to the convulsive episode. The post-eclamptic pre-eclamptic is not a good risk. Besides the possibility of a second attack of convulsions, there is a real danger to the fetus in utero and, in my opinion, an increased probability of the patient being left with permanent vascular damage. In this regard it seems appropriate to state that in other follow-up studies the incidence of vascular damage has been much higher than is the case in Dr. Arnell's series.

DR. FREDERICK H. FALLS, Chicago, Ill.—The paper of Dr. Huber clearly indicates the disastrous effects of delay in starting the management of eclamptogenic toxemia. Adequate prenatal care would have eliminated most of the cases from the convulsive group. As long as this type of case continues to be dumped in on the attending staff of clinics, just as long will these patients fail to make recoveries. The situation is analogous to what occurred in typhoid fever in the days before the pathology of this disease was understood. Patients were allowed to eat whatever they wished and a certain percentage of them developed a perforated typhoid ulcer. Those who had this serious complication very frequently died because they were untreated until the rupture occurred, and then all the surgical skill in the world was of little avail.

The patients with eclamptogenic toxemia that is permitted to go to the convulsive stage of the disease is the victim of neglect. She or her physician may be responsible for the neglect, and the responsibility may be great or small depending on whether the toxemia was slowly developing or fulminating in its onset. The solution lies, therefore, as was suggested in the paper, in furnishing sufficient prenatal care to detect the advent of serious symptoms before the convulsive stage arises. This can be done in all but a very small percentage of

cases (the fulminating variety). We are pessimistic about the medical management of these cases from the start, and we do not temporize. If the baby is alive, the uterus is opened from above just as rapidly as we can provide proper facilities for operating. If the baby is dead, we do not operate since we feel that the cause of the disease is removed (leakage of toxins from placenta) and that medical management will handle the toxemia satisfactorily. Thus, we avoid, if possible, all very real dangers of operating on these toxemic women. Dr. Huber's suggestions would be more convincing if he had done cesarean sections on some of these cases.

I have done cesarean section in 49 cases of eclamptogenic toxemia which were of the fulminating type or which had failed to respond to medical management and were, therefore, developing into severe toxemias. There were no deaths in this series. Thirteen of these patients had convulsions either during, before or after delivery. These are part of my series of 1,200 eclamptogenic toxemias in which I had a mortality of 0.6 per cent for the mothers and a gross fetal mortality of 11.9 per cent.

These patients were all clinic cases in a teaching hospital. All were handled by the resident staff according to a simple management including bed rest, saline catharsis, milk diet, and, in relatively few cases, glucose and magnesium sulfate parenterally. I am not convinced of the desirability of large doses of hypertonic glucose, and I am definitely opposed to blood transfusion in eclamptics unless absolutely necessitated by severe anemia. I think anyone who has taken the trouble to study the coagulability of the blood in eclamptics will agree that the hazards of fluid transfusion are greatly enhanced. I do not think that the Rh factor can explain all of these untoward reactions, although it may be responsible for some.

The incidence of symptoms of cerebral hemorrhage in 6 cases is worthy of note. This complication is hardly mentioned in most of the literature. However, Dr. Jaffé stated that at autopsy in eclamptics he found this frequently as the cause of death. There are not enough complete postmortem examinations being done on women dying of eclampsia, to complete our knowledge on this subject.

Dr. Arnell's paper stresses the importance of conservative medical management also, but I am in some doubt about his figures. He states that during the five-year period, 162 women with convulsions were admitted to the obstetrical service but that only 120 of them were eclamptics. However, he bases his statistics on a group of 142 cases of eclampsia. I should like to ask if there were any deaths in the 42 cases classified as not eclamptics, and if so was an autopsy performed, and if so what were the findings.

According to our experience, the eye ground findings in toxemias of pregnancy are of comparatively little diagnostic or prognostic value in the immediate handling of a given case. We have repeatedly put the eye consultant on the spot, so to speak, and he has not been able to contribute much to the management of the case.

On the other hand, I am convinced that the kidney function test which Dr. Arnell thinks of little or no value is of considerable value in the preconvulsive stage of eclamptogenic toxemia, and I think that it would be of value in managing the postconvulsive stage that he describes, preceding the onset of labor.

Spinal drainage, as recommended by Koenig many years ago, has been tried and given up. Its use is dangerous because of the possibility of sudden death from herniation of the brain down through the foramen magnum when the pressure is reduced from below. An additional danger is the breaking off of a spinal needle if the patient has a convulsion while the needle is being inserted or is in place.

Nasal oxygen has a real place in those cases showing marked pulmonary edema. Lowering the head to promote pulmonary drainage is open to question, since it increases intracerebral pressure.

Contrary to the experience of Dr. Arnell, we have found venesection an extremely valuable procedure in eclamptic convulsions, and only contraindicated in patients with a definite anemia. If we are to operate, we usually postpone the venesection until we know what the operative blood loss is, and then supplement it if necessary. We aim at the removal of about 500 c.c., since lesser amounts are usually of little avail.

This is a remarkable series of cases of convulsive toxemia without a death and in spite of my leaning toward radical treatment of the fulminating case leaves me in doubt as to its necessity if such results can be obtained by a more conservative management.

DR. KARL M. WILSON, Rochester, N. Y.—I would like to ask the authors whether they have any observations on the plasma protein in their severe toxemia cases? In some of these, the plasma proteins of course may be well below the edema level. When that is the case, the seriousness of the situation is of course aggravated, but at the same time I have been quite impressed with the results obtained by building up the plasma protein level. This can be done in three ways: (a) By the administration of protein food by mouth if the patient can take it, but this will be slow; (b) more rapidly by the administration of amino acids and the subsequent building up of plasma protein in the circulation; and (c) most rapid of all by the administration of plasma transfusion.

DR. FRED L. ADAIR, Chicago, Ill.—Certain critical responsibilities have been shown by both Dr. Huber and Dr. Arnell in connection with their presentations. They both agree, I think, that primary eclampsia is lessened greatly by adequate attention during pregnancy. This has been inadequate in their series, as in other series, and I think the medical profession and the laity as a whole, are negligent in procuring this adequate care.

They both agree, as I believe, that not all types of eclampsia can be placed in the same category, that attacks differ a great deal in their severity. It has always been difficult to say what treatment is radical or conservative as these terms have no uniform meaning. I think anything that saves life or health is conservative. Consequently, in certain cases surgical treatment may be conservative and medical treatment may be radical. Both series indicate that there are certain cases so severe—and I think Dr. Falls also referred to this and agrees with this point—that they do not respond to medical treatment, and consequently, prompt emptying of the uterus is indicated in intelligently selected cases. Now this may be accomplished from below or above, but I think we have to be extremely careful in advocating such operative procedures as cesarean section in eclampsia. While in clinics under expert observation, it may be quite possible to select cases which will respond more satisfactorily to delivery by cesarean section, if such therapy should become widespread the results would be disastrous to many patients.

An important consideration is the time when these cases should be operated upon. A patient in a convulsive or comatose state is a poor surgical risk. If we can carry such a case into a phase where all the functions of the patient are less seriously disordered, it is a much safer time to do cesarean section.

There are several other points in Dr. Arnell's paper which are extremely important. First, the care of the patient should not be delegated to obstetrically inexperienced personnel as interns and nurses. Second, the care of the eclamptic patient should be continuous until the patient is safely beyond any acute episode such as a convulsion or coma. Furthermore, it seems obvious that inasmuch as

we are treating individuals and a condition which is subject to a great deal of variation, that the treatment must be individualized. This can be done best by some one who has had considerable experience in the treatment of this condition, namely, a well-trained, experienced and competent obstetrician.

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—To any one who sees a large volume of obstetric material, it is obvious that not all cases of fully developed eclampsia can be saved. Although Dr. Huber has had discouraging results with his smaller series of cases, and Dr. Arnell astonishingly good results with a larger one, the differences between these groups will probably grow less perceptible as time goes on, for a certain number of patients admitted in extremis will die, and a certain percentage will inevitably succumb to cerebral hemorrhage in any man's clinic.

However, I am of the opinion that conservative medical treatment is still the thing in eclampsia. I would hate to see a reversion to hasty surgery in these terribly ill, poor risk subjects. I wish only that Dr. Arnell had given us a more complete description of his successful therapeutic methods.

There are certain fundamental principles to be observed in the medical management of this disease which cannot be departed from too far. Convulsions must be controlled, the patient must be put at rest, edema of vital tissues must be eliminated, organs of elimination must be stimulated and not suppressed, respiration and oxygen transportation must be encouraged.

Since following Professor Jesse O. Arnold at the Temple University, I have had the privilege of observing first hand the results of a dehydration therapy which he and Temple Fay developed at that institution. With few modifications (notably the addition of protein to dietary intake) we have followed their procedure. You may remember that the method calls for only enough morphine to gain preliminary control of the patient. Dehydration, and incidentally further sedation, is achieved by spinal puncture, intravenous hypertonic solutions, and active purgation. The objection to spinal puncture in these cases has appeared more academic than practical. Oxygen is administered freely. Particularly avoided are the barbiturates and their depressing effect upon respiration and oxygen exchange.

Of course, eclampsia itself is a rather rare disease in the larger northern cities, and we have had comparatively few cases in the past four years. However, in these I have been most favorably impressed with the treatment described.

DR. HUBER (closing).—Replying to Dr. Wilson's question concerning the plasma proteins, we have routinely made determinations upon our patients with toxemia of pregnancy and in general the level has been on the low side of normal. There did not seem to be a significant difference in the level in patients with severe or mild eclampsia.

I am very glad that Dr. Adair pointed out that there are great variations in what may be termed severe eclampsia. I am convinced that in this series, the group represented a degree of severity that is out of proportion to that which is usually classified as severe. Most of these patients are to be looked upon as patients who were neglected cases of severe eclampsia and our problem was primarily that of salvaging as many mothers and infants as possible where the prognosis was already very poor. It was from that point of view that the paper was presented.

DR. ARNELL (closing).—Replying to Dr. Falls' question regarding the source of the material requires the explanation that eclamptic admissions to two hospitals were under our management. The series embraces 142 consecutive cases and includes all cases of eclampsia admitted to our services during the period

under consideration. Convulsions due to causes other than toxemia were mentioned to emphasize the point that pregnancy with convulsions does not always mean eclampsia.

Neither blood transfusion nor spinal drainage is a routine procedure in our treatment of eclampsia. However, we have found transfusion of value in treating some cases of persistent anuria as well as in combating vascular collapse and hemorrhage. In our experience, spinal drainage often has a beneficial effect on the infrequent case showing an unusual degree of cerebral irritation.

In answer to Dr. Wilson's question regarding serum protein levels, we found the average concentration definitely lower than normal, with the greatest decrease in the albumin fraction.

THE FAILURE OF THE CONSERVATIVE TREATMENT OF ECLAMPSIA*

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ECLAMPSIA is justifiably considered preventable. Its development usually indicates the failure of the patient to obtain adequate prenatal care or the failure of the physician to recognize the severity of the developing toxemia.

All patients with eclampsia do not have the same serious prognosis. The patient who develops her initial convulsion during the course of labor has, in general, a better prognosis than the patient with antepartum convulsions. The postpartum eclamptic, unless neglected, has a still better prognosis. There is, in fact, a great variation in the severity of eclampsia developing before the onset of labor so that some patients are easily controlled while others progress to a fatal termination in spite of any therapy that may be undertaken.

During the five-year period from January 1, 1938 to December 31, 1943, there were 6,994 patients delivered in the William H. Coleman Hospital, Indiana University Medical Center. There were 51 eclamptic patients during this time. This represents a gross incidence of 7 in each 1,000 deliveries. Thirty-seven of the 51 eclamptic patients were admitted to the hospital as emergencies and had not been previously seen by our staff. We accept responsibility for the development of eclampsia in the remaining 14 patients, an incidence of 2 in each 1,000 deliveries.

It is perhaps interesting to note that eclampsia appeared in our service during every month of the year but January. Thirty-six per cent of the eclamptic patients, however, were seen during the months of May and June. Only 9 of the 51 patients had had more than one previous delivery and 35 were pregnant for the first time. Eighty-four per cent were under 30 years of age.

In the total series there were 12 maternal deaths, a loss of 23.5 per cent. There were also 18 fetal and neonatal deaths, an infant mortality of 35 per cent. These results are so poor that further analysis of them is imperative.

The 14 patients who developed eclampsia after receiving prenatal care in our clinic or in the private practice of our staff formed a distinct group. Eight of them developed their initial convulsion post partum and none had more than 3 convulsions. Thirteen infants survived. The one fetal death was a stillborn premature infant delivered at 30 weeks, 12 days following the only convulsion the patient experienced. One maternal death occurred in this group.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

This patient was a 21-year-old primigravida, 6 weeks from term, who had been under hospital observation and treatment for 18 days with apparent improvement. She suddenly developed severe epigastric pain and headache and while preparations were being made for cesarean delivery, she had a single eclamptic convulsion. A living premature infant was delivered. The patient failed to respond to therapy and died eight hours after the operation.

In comparison the remaining 37 patients formed a definitely different group. They were all emergency admissions and had developed eclampsia before the onset of labor. Using the criteria suggested by Dieckmann,¹ 13 of this group were classified as having severe eclampsia. This included patients who showed one or more of the following conditions:

1. Coma.
2. Temperature of 102° F. or more.
3. Pulse rate over 120.
4. Respiratory rate over 35.
5. More than 10 convulsions.
6. Cardiovascular impairment (edema of the lungs, persistent cyanosis, low or falling blood pressure, low pulse pressure, etc.).
7. Failure of treatment to:
 - (a) Stop the convulsions or prevent their recurrence.
 - (b) Produce a urinary output of at least 700 c.c. per twenty-four hours.
 - (c) Prevent the onset of or increase in degree of coma.
 - (d) Produce a dilution of the blood as indicated by a decrease of at least 10 per cent in hemoglobin, cell volume, or serum protein concentration.

Eleven of the 12 maternal deaths were in these 13 patients as were 9 of the 18 infant deaths. Only 2 of the pregnancies in this severe group were less than 36 weeks in duration. In all but one instance, the fetal heart was present for some hours after admission. Prematurity was not an important factor in this group of infant deaths and they can be looked upon without additional exception, as due to the toxemia. There were no maternal deaths in the remaining milder 24 eclamptic patients, and of the 8 infant deaths, 6 were delivered before the thirty-sixth week of pregnancy.

The general plan of therapy in this series has been one of conservative medical management in an attempt to control the convulsions and establish an increasing urinary output. For this purpose sodium amytal in dosages from $3\frac{3}{4}$ to $7\frac{1}{2}$ grains has been given intramuscularly at intervals of 3 to 6 hours dependent upon the response. This has been supplemented by the administration of magnesium sulfate in 100 c.c. of a 25 per cent solution intramuscularly repeated as necessary following convulsions. Rarely morphine sulfate gr. $\frac{1}{6}$ to $\frac{1}{4}$ has been given although most of the patients have received morphine before admission to the hospital, and some have received either chloroform or ether inhalations during transportation to the hospital. Intravenous 20 per cent glucose in distilled water has been given in amounts of 1,000 to 1,500

c.c. repeated 2 to 3 times each 24 hours. Where this concentration failed to increase the urinary output, or where there was cardiac embarrassment or evidence of pulmonary edema, 30 per cent or 50 per cent glucose solutions in smaller amount has been used. Continuous oxygen by nasal catheter² has been given to most patients. Veratrum veride³ has not been used. Following these procedures labor has been induced by rupture of the membranes alone or combined with the insertion of a bag, dependent upon the condition of the cervix or with the spontaneous onset of labor, it has been hastened by these procedures. Delivery has usually been performed under local infiltration or without anesthesia.

In all but the group of severe eclamptics, this general plan of management has proved effective. In the 13 patients with severe eclampsia, it has failed. Four patients died undelivered, 4 died following the delivery of stillborn infants. One patient survived following the delivery of a premature infant that died 18 hours after delivery. One mother and her infant survived. The remaining 3 infants survived following their delivery accomplished by cesarean section, which was in each instance performed upon a moribund patient. Six of the 12 maternal deaths were believed to be due to cerebral hemorrhage. This diagnosis was based upon the development of varying degrees of hemiplegia, but was proved by necropsy in only one instance. The remaining maternal deaths were associated with respiratory or cardiac failure superimposed on what are presumably irreversible metabolic changes of severe eclampsia.

It is my conviction that modification of our general plan of therapy would not have resulted in additional maternal or infant salvage. This group of severe eclamptic patients represents a failure of conservative treatment to produce any sort of satisfactory result. It is possible that any other plan of management would have been equally unsatisfactory. If we are to accept no other alternative as far as maternal salvage is concerned, there is certainly a possibility that a lessened infant mortality would result if more rapid delivery were accomplished. It seems justifiable with this in mind to undertake delivery by section in patients of this severe group. It is suggested that this be done as soon as possible following the initial establishment of conservative therapy. It is possible that termination may also result in the survival of some patients who might otherwise have been lost.

Various studies are recorded in the literature which indicate that the maternal survival is greater where operative interference is not undertaken. This is unquestionably true as regards any type of accouchement forcé. It is less definitely demonstrated in relation to cesarean section. Most reports of the use of cesarean section in the treatment of eclampsia are based on data collected more than fifteen years ago, and therefore, eliminate any improvement in technique that has occurred during that time. Most of them were sections done under general anesthesia.

Dieckmann quotes data from 3 large obstetric clinics showing that the maternal mortality increases from 7 per cent if delivery occurs within two hours of the first convulsion to 28 per cent if more than 21 hours elapse. He also states that, as a rule, where labor is slow, the eclampsia is likely to become more severe resulting in a higher maternal mortality. There seems no justification for the consideration of cesarean section in those patients with eclampsia who respond well to medical management and in whom labor progresses rapidly. There does seem to be justification for the consideration of it in those patients who fail to respond to conservative management and in whom the eclampsia had progressed to the severe stage.

The most satisfactory approach to the problem presented by this group of patients is the earlier recognition of the developing toxemia and the institution of adequate treatment before convulsions develop. It is significant in this connection, that in this series of patients with severe eclampsia, there had been little or no prenatal management. Many of them were seen by their local physician for the first time after convulsions had occurred. In all of the remainder the prenatal care had been inadequate. The majority of these patients came from an area essentially rural, and were of a relatively low economic level. They demonstrate the continuing need for additional public health and postgraduate medical education.

It seems logical to make the following conclusions from a study of this series of patients.

1. Conservative medical management followed by vaginal delivery is recommended for the treatment of mild eclampsia.

2. Adequate prenatal care, if it does not prevent the development of eclampsia, decreases the severity of the process and greatly improves the chance of survival of mother and infant.

3. Conservative treatment of severe eclampsia gives unsatisfactory results.

4. In severe eclampsia, the infant survival rate would be materially increased by the performance of cesarean section within a few hours following the institution of conservative medical management.

5. In severe eclampsia, the maternal survival rate is so negligible that the performance of cesarean section is justified in the interests of the infant and might be favorably influenced by the more rapid completion of the delivery.

6. Additional public health and postgraduate medical education is essential for the adequate prevention and control of eclampsia.

References

1. Dieckmann, W. J.: *The Toxemias of Pregnancy*, 1942, The C. V. Mosby Company, St. Louis.
2. Nicodemus, R. E.: *J. A. M. A.* 117: 1238, 1941.
3. Bryant, R. D., and Flemming, J. G.: *J. A. M. A.* 115: 1333, 1940.

A STUDY OF 250 CASES OF PLACENTA PREVIA*

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ALTHOUGH significant improvement in its treatment has been made in the past twenty-five years, placenta previa still remains one of the major obstetric problems, as little or no light has been shed upon its preventability, or etiology. That obstetrics is not an exact science, and cannot be practiced by formulas, can be no better illustrated than in the treatment of cases of implantation of the placenta in the lower uterine segment. In cases apparently identical in their inception, the end results with like treatment may be far apart. It is by interchange of experience among us that improvement is made, and even then what is one man's meat may be another man's poison, in so far as the application by the individual obstetrician of various procedures in treatment is concerned. It is with this in mind that I am presenting for your consideration and criticism, our experience for a period of ten years in the management of placenta previa.

Material

The material for this review is composed only of proved cases of placenta previa, and consists of patients encountered with this complication in a period of ten years, 1933 to 1942. In order that an adequate cross section of patients of widely varying economic and social status may be obtained, it is taken from the obstetric divisions of two hospitals, with different types of clientele. Harper Hospital is a private hospital with a small percentage of nonpay patients, while at Herman Kiefer Hospital, all cases are of the kind that require public assistance and are used for teaching purposes.

Incidence

A total of 31,996 deliveries occurred during the ten-year period, and among these placenta previa was encountered in 250, an incidence of 1 in 128. A high incidence is to be expected in hospital practice according to the reports of all observers.

TABLE I. AGE GROUPS

15 to 19		20 to 24		25 to 29		30 to 34		35 to 39		40 to			
16		44		78		59		42		11			
PARITY													
<i>I</i>	<i>II</i>	<i>III</i>	<i>IV</i>	<i>V</i>	<i>VI</i>	<i>VII</i>	<i>VIII</i>	<i>IX</i>	<i>X</i>	<i>XI</i>	<i>XII</i>	<i>XIII</i>	<i>XIV</i>
49	59	41	22	32	13	6	11	7	3	0	4	2	1

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

The high percentage of cases (54 per cent) occurring in the age group 25 to 34 bears out the commonly made observation, that placenta previa occurs most in the middle childbearing period.

Our material shows that placenta previa occurs about five times as often in multiparas as in primiparas. In private hospital practice, the condition is more common in primiparas than in clinic practice. Thirty-nine cases occurred in primiparas in the former group of 101, while only 10 of 149 cases were primiparas in the clinic group.

Placenta previa seems to be more prevalent among whites. Of 250 cases only 51 occurred in colored women, in spite of the fact that our nonpay patients are comprised of a high percentage of colored.

TABLE II. LOCATION OF PLACENTA

Marginal	133
Lateral	67
Central	50
Total	250

The difficulties associated with making an accurate classification of placenta previa, according to location, need no elaboration to a group of experienced obstetricians. Every effort has been exerted in the attempt to have our grouping as nearly correct as possible. We find that 53.2 per cent were marginal, 26.8 per cent were lateral, and 20 per cent were central.

While every means advisable is used to make a correct diagnosis of the location of the placenta, we believe that the amount of blood lost, or being lost when the patient is first seen, should be a better guide to treatment than the amount of os covered by the placenta. In our experience, more blood is lost, at times, with the marginal than with the central type.

TABLE III. CONDITION OF PATIENT

	GOOD	FAIR TO POOR	VERY POOR
Vaginal delivery	90	78	23
Cesarean section	42	16	1
Total	132	94	24

Of paramount importance in treatment and prognosis, is the condition of the patient when first seen. Table III gives our estimate in the 250 cases studied. Those classified as "Good" had no serious blood loss, as shown by clinical observation, pulse rate, blood pressure, blood count, hemoglobin readings, etc. Those called "Fair to Poor" have had sufficient loss of blood so that their condition can readily be discovered clinically, and confirmed by laboratory findings. We have classified as "Very Poor" those patients entering in really serious condition with massive blood loss, marked pallor, rapid thready pulse, frequently with air hunger, with hemoglobin readings below 50 per cent,

and with marked drops in blood pressure. I believe it is significant that of the women treated by cesarean section, only one case was in this "Very Poor" group.

Symptoms and Diagnosis

Painless, causeless bleeding, particularly if occurring in the last trimester of pregnancy, is the classical symptom, and has been invariably present.

I do not believe it necessary or advisable to confirm a diagnosis of placenta previa in all cases by vaginal examination; and particularly in those in which delivery by cesarean section is contemplated. A sufficiently accurate working diagnosis can be made in many instances by other means.

Two aids to diagnosis I have found to be of considerable help; viz., the location of the placental souffle, and the use of the x-ray.

If heard best low in the abdomen above the symphysis, in cases with suspected placenta previa, I think the location of the placental souffle to be of considerable significance. While attempts are always made to locate it, these are easily omitted from the written record which accounts for the fact that I have record of them in only 71 cases. Of these, it was heard low above the symphysis in 59, and not heard in 12.

X-ray diagnosis was attempted in 32 cases, proved to be placenta previa, by the use of an opaque medium in the bladder, or by the soft tissue technique. In 24, a positive confirmatory diagnosis of placenta previa was made, in 3 the diagnosis was questionable, and in 5 negative. A correct diagnosis was made in 75 per cent of patients.

TABLE IV. METHOD OF DELIVERY

<i>Vaginal</i> 191	
(A) Expectancy	58
(B) Rupture of membranes	26
(C) Bag insertion	105
(D) Braxton Hicks' version	2
<i>Cesarean Section</i> 59	
(A) Classical	10
(B) Low cervical	44
(C) With supravaginal hysterectomy (Porro)	5

It is evident from Table IV, that widely varying methods of delivery have been used. This I think is to be expected in any series of cases that represents a true sampling of a large metropolitan population. Our patients come from all social and economic levels, and their condition when first seen precludes treatment of a single type. In this connection it is interesting to note that in 101 placenta previa cases from Harper Hospital, cesarean section was the treatment of choice in 41, while in 149 cases from the Herman Kiefer service, only 18 cases of section occurred.

Patients of private physicians, who have had adequate prenatal care, and who are seen with the first bleeding are much more likely to be

candidates for section, than nonpay patients who frequently enter in serious condition. All the more is this likely to be true if the patients are paras i or ii, at or near term, with both mothers and babies in good condition.

Four of six attending obstetricians at Herman Kiefer Hospital also do their private obstetrics at Harper Hospital, enough I think to appreciably influence the trend of treatment over a period of ten years. And yet, these men, who have a comparatively high cesarean rate in private practice, do not throw their influence toward a higher rate at Herman Kiefer Hospital. Again the answer is found in the types of material encountered, regardless of the comparative simplicity of treatment by the abdominal route. That good results for both mother and child with cesarean section are obtained, will be shown in our mortality tables, but only, I believe, when we do not overstep the bounds of sound surgical judgment.

Preference for the low cervical operation is marked, 44 of 59 cesarean sections being of this type. There have been no serious technical difficulties and we agree with Greenhill and others, that at times, the low incision is of distinct advantage in the control of bleeding from the placental site.

In delivery by the vaginal route, "expectancy" was chosen as most appropriate for 58 mothers and 59 babies. By expectancy we mean that no active treatment, aimed at delivery, was instituted, and labor was allowed to continue, under close observation, until complete dilatation of the cervix. From then on, labor was terminated according to indication. Thus, spontaneous delivery occurred in 40, forceps in 10, version and extraction in 5, and breech extraction in 4. Of 26 patients in whom rupture of the membranes was the only active treatment in the stage of dilatation, labor terminated spontaneously in 11, forceps were used in 2, version and extraction in 8, and breech extraction in 5.

The insertion of the dilatable bag for control of hemorrhage, and to aid in dilatation was thought to be the best treatment for 105 women, and 110 babies. After which delivery was spontaneous in 64, forceps delivery was done in 9, version and extraction in 14, and breech extraction in 18.

I am fully aware of the criticisms that have been aimed at the use of the bag and its many supposed disadvantages, such as predisposition to malpositions, inefficiency in control of hemorrhage, infection, etc., and can only say that these have not occurred to an extent to discourage us in its continued use. Malpositions after the use of the bag have occurred so infrequently, as to be statistically unimportant. Control of hemorrhage has been excellent, and I have found no case of failure while the bag was in situ. While infection is a well-known complication of placenta previa, in general, I have found no increase in morbidity after the

use of the bag as compared with other methods of treatment with delivery from below.

On the other hand, I am confident that in many cases entering as emergencies, with massive blood loss and profuse bleeding, the insertion of the bag has controlled hemorrhage to permit of blood transfusion and other supportive measures which have been lifesaving. It is of little use in these cases to allow the patient to lose blood faster than it can be replaced. The use of the bag is a more exacting form of treatment from the viewpoint of the obstetrician than is cesarean section, as it requires constant attention to detail and indefinite periods of waiting for its expulsion. Serious bleeding can occur above it, unobserved externally, if it is not promptly removed once its purpose is served. Of value in vertex positions, particularly, is the use of small doses of pituitrin, once the bag is removed, to help wedge the head firmly against the placenta, or careful version and slow extraction can be done to advantage in many cases. If the placenta does not separate immediately it is removed manually, followed frequently with the insertion of a gauze pack.

I have no fault to find with the obstetrician who can limit his treatment of placenta previa to simple rupture of the membranes and cesarean section. As has been seen, we use both these methods. However, in our material, there is a group of cases which is not suitable for either of these; for them we use the dilatable bag.

TABLE V. MORBIDITY AND MORTALITY

By the commonly used criteria 78 cases were morbid post partum, 31.2%; maternal mortality, 7—2.8%; vaginal delivery, 6—3.1%; cesarean section, 1—1.7%.

PARA	DURATION	CONDITION	DILATATION	PLACENTA	TREATMENT	CAUSE OF DEATH
(1) iv	6½ mos.	Very poor	Complete	Centralis	Rupt. Memb. V & E	Transfusion reaction
(2) iv	7 mos.	Very poor	Complete	Centralis	Rupt. Memb. Spont.	Hemorrhage
(3) iv	9 mos.	Fair	4 cm.	Lateralis	Bag, V & E	Not known, autopsy, Anesthetic (?)
(4) iii	9 mos.	Poor	2 cm.	Centralis	Low cervical section	Acute dilatation of heart, circulatory collapse
(5) vi	9 mos.	Poor	5 cm.	Lateralis	Bag, Breech ext.	Hemorrhage
(6) ii	6½ mos.	Fair	4 cm.	Lateralis	Bag, V & E	Hemorrhage
(7) iii	8 mos.	Very poor	6 cm.	Centralis	Bag, Breech ext.	Septic pneumonia 12th day

A total of 7 cases died, 6 after vaginal delivery, and 1 after low cervical cesarean. Reference to Table V will show, in more detail, the facts pertinent to these cases. One case dying after transfusion, and one probable anesthetic death possibly could have been avoided. In the case of the posttransfusion death, the Rh factor was not determined which, in the light of later knowledge, might have accounted for it.

Of the total of 250 cases delivered, 263 babies were born. There were 13 twin pregnancies, and 4 malformations incompatible with life, a high incidence, confirming the experience of most writers—91 babies did not survive, a gross mortality rate of 34.6 per cent.

There were 56 neonatal deaths, of which 31 were nonviable prematures, and 3 had malformations incompatible with life.

Thirty-five babies were stillborn, of which 18 were nonviable prematures, and 1 had malformation incompatible with life.

TABLE VI. FETAL MORTALITY

Total deliveries:	263
Total deaths:	91
Gross rate:	34.6%
Neonatal deaths:	56
Nonviable prematures	31
Malformations	3
Total nonviable	34
Stillborn:	35
Nonviable prematures	18
Malformations	1
Total nonviable	19
Net fetal death rate	14.4%

It is a questionable procedure to arrive at a net fetal mortality rate for placenta previa, because prematurity and fetal malformations are an inherent part of the risk in this complication of pregnancy. However, if the usual practice is followed and the above deductions are made from the gross death rate, it is found that 34 babies born alive and 19 stillborn were nonviable, a total of 53. Thus, the net fetal death rate is 38 or 14.4 per cent.

Discussion

No discussion of placenta previa in modern times is complete without reference to blood transfusion, and the use of blood plasma. Their use with us is so common as to be routine in all but the mildest cases of bleeding. Patients have received at times, before, during, and after delivery, as much as 3,000 to 3,500 c.c. of blood. While plasma is very valuable, it does not fill the place of whole blood in cases with massive hemorrhage. There is considerable time consumed in typing, cross-matching and Rh factor determination while the patient continues to bleed. The use of plasma during this period is a valuable adjunct. At times, washed red cells have been used. All cases of suspected placenta previa should have the benefit of hospitalization, and blood for transfusion should be available for them. Bill of Cleveland was among the first to call our attention to the reduction in mortality possible when these conditions are fulfilled.

Apparently, the best results in the treatment of placenta previa are obtained by the obstetrician in the care of his private patients (mor-

tality 1.9 per cent). The intelligence of the individual patient is an important factor. Many tragic cases are the result of failure of the woman to report mild bleeding in the last trimester to her clinic or to her physician.

We have had no experience with Willetts' scalp traction but from the reports of experienced observers, believe that it has merit in properly selected cases, and intend to try it when the opportunity presents itself. One academic objection to its use in the case of prematurity might be the difficulty of application of the forceps to the snugly fitting scalp of a premature infant.

In studying placenta previa in a metropolitan area, I believe it important that sampling, as widely as possible, in all social and economic strata, be done. For this reason, material from two hospitals with widely varying types of clientele has been studied. This analysis shows marked difference in treatment, especially in the use of cesarean section. That this occurs with staffs that, to a large extent, are interlocking, and where the attending obstetrician is free to exercise his own best judgment, leads to the conclusion that treatment must vary greatly with the conditions encountered, considered in the broadest sense. I believe that each case should be individualized. The obstetrician should have an open mind, free from prejudice in favor of one or another form of treatment. Treatment should conform to the immediate need of the patient, and should not be based on preconceived ideas of the operator.

Summary

For a ten-year period, 1933 to 1942, there were 31,996 deliveries at Harper and Herman Kiefer Hospitals, among which there occurred 250 cases of placenta previa, 1 in 128.

Placenta previa is found in primiparas and multiparas in the ratio of 1 to 5.

It is more common in whites than colored.

It occurs most commonly in the middle childbearing age.

A high percentage of twin pregnancies and fetal malformations is to be expected.

A large group was satisfactorily managed by expectant treatment during the stage of dilatation, or by simple rupture of the membranes.

The insertion of the dilatable bag gives good results in cases adapted to its use.

In properly selected cases cesarean section can be used to the advantage of both mother and child.

Seventy-five per cent of cases were correctly diagnosed by x-ray in the group in which it was used.

Blood transfusion should be available to all patients with placenta previa. An acceptable mortality rate cannot be expected without it.

Maternal mortality in 250 cases of placenta previa taken from a large metropolitan area was 2.8 per cent.

Gross fetal mortality was 34.6 per cent, net 14.4 per cent.

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Discussion

DR. T. K. BROWN, St. Louis, Mo.—Cases of pregnancy with painless, causeless uterine hemorrhage in the last trimester should be hospitalized as soon as possible with the tentative diagnosis of "Placenta Previa." The diagnosis should be confirmed promptly by history, physical findings and perhaps roentgenological methods. Treatment should be instituted at once with the following purposes: (1) arresting hemorrhage; (2) emptying the uterus as promptly as is safe; (3) insuring control of hemorrhage after delivery; (4) counteracting anemia; (5) preventing infection.

Hemorrhage may be arrested by the administration of vitamin K, rupture of the membranes, insertion of a bag or cesarean section. The uterus may be emptied as promptly as is safe by rupture of the membranes, insertion of a bag or cesarean section. Hemorrhage after delivery may be controlled by drugs, packing, and perhaps suture of the placental site. Anemia should be counteracted by the transfusion of Rh negative blood before, during, and following delivery. Plasma transfusions may be used to combat "shock" but do not supply the necessary cellular elements to correct the anemia. Infection may be prevented by the use of proper technique, administration of vaginal antiseptic instillation, limitation of interference to a minimum, and removal of any pack in eight to ten hours.

Watson and Gusberg have recently reported definite improvement in maternal and fetal mortality and maternal morbidity by the use of cesarean section in the treatment of placenta previa in comparison with their results following use of the bag.

In the analysis of Dr. Seeley's cases, central placenta previa was encountered in 1 out of every 5 cases. In such cases, delivery by cesarean section is the method of choice.

As to the condition of the patients when first seen, 20 per cent were classified as "very poor" but only one case in the group was delivered by section. Would it not have been possible to have improved the condition of these patients by proper treatment and then to have delivered some of them by cesarean section?

Over 50 per cent of this series of cases was treated by the insertion of a bag. I still fear the danger of infection associated with the use of a bag. The fetal morbidity for the 250 cases reported was 31.2 per cent. Was there any difference in morbidity in the group that was "bagged" as compared with the remainder of this series?

Marginal placenta previa was reported in 133 patients. Nevertheless, only 26 cases were treated by rupture of the membranes. It would seem that this method of treatment could have been employed frequently.

Among 101 private patients, of whom 39 were primigravida, 41 cesarean sections were performed. These patients were in good condition and the results could be expected to be satisfactory. In contrast, among the 149 clinic patients, of whom 10 were primigravida, only 18 cesarean sections were performed. Perhaps in this latter group the indication for cesarean section could be broadened and used as the method of delivery after proper prophylactic treatment.

Low cervical section was performed in 44 instances among the 59 cases delivered by section. One must consider the increased hazard of encountering the placental site at operation in this particular group of cases. The loss of blood may be

increased definitely and perhaps to a dangerous degree. By the use of classical section this difficulty may be obviated. However, the placental site might be sutured, if necessary, more readily after low cervical section. Postpartum bleeding can usually be controlled by the use of a pack.

Dr. Seeley and his co-workers are to be complimented on their satisfactory maternal mortality rate of 2.8 per cent and should continue to individualize the treatment of their cases of placenta previa in the future.

DR. EDWARD A. SCHUMANN, Philadelphia, Pa.—The whole subject of placenta previa continues, even after the hearing of this excellent paper, in my mind as the most confused chapter in obstetrics. Neither the cystogram with an opaque medium nor the soft tissue x-ray has proved satisfactory as a diagnostic method in our hands except as corroborative evidence in well-established cases. The diagnosis by vaginal examination has even offered difficulties to me. If one passes a finger through the cervical canal one can tell, but who dares? As to the difference between a lateral and marginal position, this is often merely an academic decision.

When we come to the subject of treatment the chapter becomes still more confused. I would be very happy to have outlined to me the treatment of placenta previa in a woman six and a half months pregnant who desires a child. I know of no satisfactory treatment except expectancy, which sometimes is feasible and sometimes not. Given the case of a primipara shortly before the viability of a child, when the child is desired by both parents, I think it is the duty and necessity of the obstetrician to lay the dangers of expectant treatment clearly before the parents and have them make the decision as to whether the woman should be permitted to go on with her pregnancy facing the danger of a severe hemorrhage. The full responsibility should be placed on the parents.

As to the treatment of placenta previa after the viability of the child, I would accept the form of treatment that best suits the capability of the obstetrician. In my own cases, I am more influenced by the condition of the cervix than any other factor. Given a soft or partially dilated cervix I believe any of the methods of treatment will be successful and will give the excellent results produced by Dr. Seeley. Where the cervix is dense and does not render itself easily dilatable, I think cesarean section is the only method. In a member of my own family, cesarean section would be practiced almost invariably with a viable child and a placenta previa.

DR. JOSEPH L. BAER, Chicago, Ill.—I have been waiting for some one to emphasize the fact that obstetric hemorrhage has displaced puerperal infection as the number one cause of maternal deaths in the United States. Not having heard it, I again bring it to attention. For many years all of the specialty societies, including this one, have been emphasizing the educational needs for the prevention and treatment of puerperal infection, which now has taken second place. It now behooves us to embark on a more vigorous program of education for the men in general practice who are the ones to see the patients with premature separation of the placenta and placenta previa. We must emphasize first the extreme importance of bleeding in the third trimester of pregnancy so that those patients will be immediately hospitalized and be given the benefit of early expert consultation. If that can be accomplished, we will definitely lower our maternal mortality from obstetric hemorrhage.

Vaginal examination is not merely permissible but highly desirable. Of course, in the delivery room precautions must be taken against the possibility that the examination will precipitate further bleeding. The sensation given by a thickened area in the lower uterine segment between the finger and the presenting part, which in these patients can usually be impressed into the pelvis, since the infants are so frequently premature, is definite evidence of the low implantation. Subse-

quent treatment then is a matter of individual choice. In many instances simple rupture of the membranes with adequate drainage of the liquor amnii should take precedence over the abdominal approach.

DR. F. H. FALLS, Chicago, Ill.—I should like to ask how one would differentiate between placenta previa and carcinoma of the cervix without a vaginal examination? X-ray in placenta previa in our hands has been very unsatisfactory.

Inserting a bag to facilitate the delivery in placenta previa increases the danger to the fetus from compression of the placenta by the bag. This is particularly so if the cord happens to be inserted at the lower side of the placenta, for in that event when the bag is blown up, you stop the circulation of the cord.

When doing a low cervical cesarean section for placenta previa, you may cut through the placenta and thus divide the large vessels of the fetal surface. This is analogous to cutting the baby's throat, and from under such circumstances you have to hurry to get the baby out and the cord clamped in order to prevent bleeding. This is an important cause of fetal death. In a good many of these cases there may be justification for doing a classical operation thus avoiding injury to the placenta by the knife.

My last point concerns the cause of the bleeding in placenta previa. We think it is associated with the contraction of the uterus and the formation of the lower uterine segment. We believe that if there were a way of stopping the contractions, we might reduce the chances of full separation of the placenta. In the last five or six years, therefore, we have been giving progesterin until viability of the baby was attained and then doing a cesarean section.

DR. FRED L. ADAIR, Chesterton, Ind.—The advocacy of expectancy or delay in treating placenta previa is extremely hazardous, and if generally adopted would lead to an increased mortality. It should not be carried out under any circumstances except in a special hospital and with expert care.

We have felt at the Chicago Lying-in Hospital that rectal examinations are never justified in placenta previa and that when a vaginal examination is made, it should be done as promptly as possible with everything in readiness to take care of the case by the most expert treatment. In many cases, however, the very simple procedure of rupture of the membranes is of great value in the management of these cases.

DR. GEORGE W. KOSMAK, New York, N. Y.—In closing I would like Dr. Seeley to state whether the insertion of the bag was extra- or intraovular.

DR. SEELEY (closing).—In advocating the use of the dilatable bag, I might remind you that the majority of our cases in which it was used were brought to us by ambulance and showed more than 4 cm. of cervical dilatation. A large proportion of them are multiparas and I do not know any way of controlling the hemorrhage except by the use of the bag. If you could see our material I think you would doubt that they were cases for cesarean section.

Replying to the question as to infection after the use of the bag, I would say that we have not been able to show any more morbidity with the use of the bag as compared with other methods for delivery from below. All of our men except one have favored the use of the intraovular bag. The extraovular bag has been used in a certain percentage of these cases, the argument being, of course, that the extraovular bag would be likely to give a lower percentage of fetal deaths.

AN ANALYSIS OF STERILITY STUDIES IN THE FEMALE*

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THE problem of sterility is an age old one, as is evidenced by the frequent references to barrenness in the biblical literature and there are probably few afflictions that cause as much anxiety and unhappiness as does this condition. It has been estimated by Reynolds, Macomber, and Lotka that 13 to 17 per cent of the marriages in this country are barren. This seems like a high incidence in these days of scientific achievement and in this world of plenty. Nevertheless, it is true and should serve as a real incentive to the medical profession to put forth every effort to correct and overcome, in so far as is humanly possible, the varied causes of sterility.

Prior to 1920, sterility studies in the female were often cursory and not too scientific. The usual procedure then, was a pelvic examination to determine and correct, if present, any uterine displacement. Often a dilatation and curettage was carried out, but not for any sound scientific reason. Little emphasis was placed on the male as a possible causative factor. But all these things have changed and in the last quarter of a century, more has been accomplished to overcome sterility than in all the centuries preceding it.

The world of today is especially in need of an increased number of births, to replace those that have and will be called upon to make the supreme sacrifice to bring us total victory. So we feel that every one of these discouraged couples, that come to us with their problem of infertility, should be given the greatest consideration and the benefit of our best and most complete scientific investigation.

The purpose of this presentation is to analyze a group of seventy-six women, who were admitted to our clinic at the Geisinger Memorial Hospital in the two-year period ending July 1, 1943, with the chief complaint of inability to conceive.

All but five of the husbands of these women, were examined by our urologist or by a competent physician elsewhere prior to the admission of their wives for studies. Of the remaining seventy-one husbands, sixty-eight, or all but three, were reported as having an ample number of motile spermatozoa with good morphologic characteristics, which according to Rubin and others, pretty nearly exonerates the male from being responsible for the infertility. The probable causes for the sterility in the three husbands pronounced infertile were reported as chronic prostatitis, absence of spermatozoa, and diminished motility of spermatozoa with a high incidence of abnormal forms, respectively.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

These findings do not seem to bear out the works of Mazer, Israel, and Charny who found in their series that 40.6 per cent of the male partners had various types of semen abnormalities and, therefore, were potentially a factor in their barren marriages.

Suffice it to say that the sixty-eight husbands who were reported to have normal semen received no therapy. The three husbands, who were found infertile received active treatment for a long period of time on the urological service and it is interesting to note, that to date, no pregnancies have resulted in these three couples.

From this point on, our chief concern on the gynecological service was the study, evaluation of our tests, and the treatment of these seventy-six women admitted to our hospital complaining of infertility. Their ages varied from 21 to 38 years, the average age being 28.3 years. The period of marriage varied from 1 to 19 years, or an average of 5.8 years. The period of infertility varied from 1 to 19 years and the average for the group was 4.9 years. Two patients showed evidence of anemia and only one had a positive serologic test. Of the entire group, only 21 patients gave a history of irregular menses or menstrual disturbance. Twenty-one patients had one previous pregnancy which resulted either in a full-term baby or abortion followed by at least two years of sterility.

A careful pelvic examination by palpation and inspection was carried out in each instance and the following conditions were revealed.

TABLE I. PELVIC FINDINGS

1. Normal pelvis	45
2. Genital hypoplasia	8
3. Retroversion	4
4. Uterine fibromyomata	3
5. Adnexal pathology	13
6. Cervical stenosis	3
Total	76

Three of the patients had previous pelvic surgery which may or may not have played some part in their sterility. From these examinations, it would seem that 45 patients or nearly two-thirds of the series had normal pelvic organs, as far as could be determined, by manual palpation and inspection. Those patients with genital hypoplasia were treated with estrogenic substance and thyroid extract. The four patients with retroversion had manual correction and pessaries were inserted. The three patients with a diagnosis of fibromyomata were advised at least for a time against surgery because of the small size of the tumors.

The diagnosis of adnexal pathology occurred thirteen times and included cystic ovaries, thickened and fluctuant Fallopian tubes, but no evidence of any acute pelvic inflammatory disease. None of these existing adnexal conditions had caused the patient enough pain or distress to have suggested their presence, nor were they of such a

nature that surgical measures would likely have lessened their sterility. Cervical stenosis occurred in three patients and all were dilated with graduated dilators.

An attempt was also made to classify the entire group according to endocrine status and the following table represents this correlation.

TABLE II. ENDOCRINE STATUS

1. Normal	24	31.5%
2. Hypothyroidism	36	47.4%
3. Pituitary dysfunction	5	6.6%
4. Ovarian dysfunction	11	14.5%
Total	76	100.0%

Of the group, 24 had no symptoms nor physical evidence of any endocrinopathy.

Hypothyroidism comprised the largest single group, in fact almost half of the entire series. It is interesting to note, that in most instances, we were able to pick out the hypothyroid cases simply by careful interrogation before the basal metabolic determinations were computed. These patients have a definite syndrome and practically all of them had the characteristic signs and symptoms of fatigue, lack of energy, sensitivity to cold, inability to get up in the morning feeling rested, dry, lusterless, and straw-like hair, deficient vaginal secretions, and absent or diminished libido. The basal metabolic determinations for these patients were characteristically low, varying from -7 per cent to -33 per cent, the greater number varying between -15 per cent and -20 per cent. Twenty-nine of the 36 hypothyroid patients had basal metabolic rates below -10 per cent and the other 7 patients had rates varying between -10 per cent and 0. It may be said here, that in our opinion, a -10 per cent basal metabolic rate, which is considered a low normal by most schools, is in reality quite subnormal and clinically capable of producing the characteristic hypothyroid syndrome, with the resultant sterility. Therefore, for all practical purposes, the minimum normal basal metabolic rate should more nearly approach zero. The treatment prescribed for the hypothyroid group was desiccated thyroid extract grs. ss b.i.d. to grs. I t.i.d. varying with the size of the patient, severity of symptoms, and the degree of subnormal basal metabolism.

The five cases diagnosed pituitary dysfunction, presented the typical pelvic and shoulder girdle adiposity and in each instance their weight considerably exceeded that of all others in the series. One patient received x-ray radiation of the pituitary at another hospital. Two patients received a series of gonadogen injections, and one patient refused treatment while the fifth one had regular menses and no hormone therapy seemed indicated.

The ovarian dysfunction group totaled eleven patients, eight of whom had definite hypoplastic genitalia and, in most instances, had

menstrual irregularities. These patients received estrogenic therapy in the form of stilbestrol 2.0 mg. three times a week and small doses of thyroid extract in the amount of grs. ss t.i.d.

The hysterosalpingogram was done on twenty-one patients to determine patency of the Fallopian tubes with the following results.

TABLE III. HYSTEROSALPINGOGRAMS

DIAGNOSIS	NUMBER	SUBSEQUENT PREGNANCIES
1. Patent tubes	10	6
2. Occlusion of one tube	3	2
3. Occlusion of both tubes	7	1
4. Partial stenosis	1	1

The incidence of pregnancy which ensued in this group, when the uterosalpingogram was done, seemed quite high and possibly cannot have too much importance attached to it because of the small number in the series.

Tubal insufflation, or the so-called Rubin test, was performed on forty-five patients and the following kymographic interpretations were recorded.

TABLE IV. TUBAL INSUFFLATIONS

DIAGNOSIS	NUMBER	SUBSEQUENT PREGNANCIES
1. Patent tubes	19	7
2. Partial stenosis	8	1
3. Bilateral occlusion	17	1

Many of these patients had repeat tubal insufflations but these are not recorded, since for practical purposes, the management of each case was carried out with respect to the initial findings. However, from the comparison of the uterosalpingograms and the tubal insufflations, disregarding the relatively small series, the former was followed by a much higher incidence of pregnancy which was not at all evident to us until this analysis was carried out.

Endometrial Biopsy

In recent years, we have learned that endometrial biopsies can be most helpful, and thus, should be an integral part of every investigation for sterility in the female. It is our practice to arrange admission of the patient for her sterility studies two or three days before the expected menstrual flow, in so far as is possible. In this way we feel, that if the patients have ovulated, it can be verified by the microscopic picture of the luteal phase in the biopsies, and thus rule out anovulatory menstruation as a possible cause of the sterility. It must be remembered, however, that many of the patients who present themselves for study have very irregular menses or possibly amenorrhea, for a long period of time. It is, with this type of case, that the endo-

metrial biopsy is of doubtful value since it permits no correlation of the menstrual cycle, and, therefore, our efforts must first be directed toward the establishment of a regular cycle with rhythmic bleeding. This we have accomplished in a few instances by the administration of gonadogen, synopodin, and prostigmin sulfate but not with sufficient success to herald it widely.

In concluding our studies and arriving at the final analysis, it was necessary to contact 27 of the 76 patients by letter and a questionnaire to determine our results, because of their failure to return for their follow-up examination. A few of these had become discouraged and consequently had discontinued their medication, but for the most part the reports were encouraging. The other 49 patients were most cooperative in aiding us in this study, even though it required traveling rather long distances every two or three months for follow-up examinations.

Table V, with the cases arranged according to endocrine status, shows our end results in the number of pregnancies obtained, including both full-term babies and spontaneous abortions.

TABLE V. INCIDENCE OF PREGNANCIES

ENDOCRINE STATUS	NUMBER	TOTAL NO. OF PREG- NANCIES	FULL-TERM PREG- NANCIES	SPONTA- NEOUS ABORTIONS
Normal	24	4	4	0
Hypothyroid	36	19	17	2
Pituitary dysfunction	5	0	0	0
Ovarian dysfunction	11	6	5	1
Totals	76	29	26	3

From these findings it is quite clear that the hypothyroid and ovarian dysfunction groups, which together total 47 patients, lend themselves well to simple therapy, as is shown by the total of 25 pregnancies that resulted, an incidence of slightly better than 50 per cent. In contrast, the pituitary dysfunction group, which was small, had no resulting pregnancies and the patients showed no benefit or improvement from our medication. In the normal group of 24 patients our results were a little better, but far from satisfactory. The women in this group probably cause us more concern than all the rest put together, for the reason that they appear perfectly normal and show none of the characteristic signs and symptoms so common in endocrinopathies and, if after eliminating such causative factors as occluded tubes, fibromyomata, etc., we have only to accept an inherent low fertility factor as the probable cause of their sterility.

We have been especially impressed with the treatment of our hypothyroid and hypoovarian groups with thyroid extract. While we know it is a form of therapy, that has been used for years and was stressed by Litzenberg in 1937, in carrying out studies on a similar series and with comparable results, yet we feel that there are many

more hypothyroid patients than most medical men are willing to admit and that the greatest number of patients to benefit and overcome their sterility is dependent upon the physician's looking more carefully into the patient's metabolic condition and resorting less often to the diagnosis of psychoneurosis. It has been our experience even though many of these hypometabolic patients may never conceive, they do improve both physically and psychically on thyroid therapy and, thereby, usually become better partners in marriage.

Summary

1. An analysis of seventy-six cases of sterility in the female.
2. The studies that afforded us the greatest information as to the cause of the sterility were basal metabolic determinations, hysterosalpingograms, and tubal insufflations.
3. The greatest number of pregnancies occurred in the hypothyroid and ovarian dysfunction groups that received thyroid extract, estrogenic therapy and/or follicle stimulating hormone.
4. Of seventy-six cases studied and treated, a total of twenty-nine pregnancies resulted, three of which terminated in spontaneous abortion, and the remaining 26 were delivered as normal healthy babies.

References

- Titus, P.: *Am. J. Surg.* 35: 345-351, 1937.
 Pommerenke, W. T.: *New York State J. Med.* 37: 1035-1041, 1937.
 Litzenberg, J. C.: *J. A. M. A.* 109: 1871-1873, 1937.
 Zuck, T. T.: *AM. J. OBST. & GYNEC.* 36: 998-1005, 1938.
 Mazer, C., Israel, S. L., and Charny, C. W.: *Pennsylvania M. J.* 41: 1009-1016, 1938.
 Meaker, S. R., and Vose, S. N.: *J. A. M. A.* 115: 1426-1428, 1940.
 Mason, L. W., and Black, W. C.: *AM. J. OBST. & GYNEC.* 39: 1022-1024, 1940.
 Huber, C. P., and Davis, M. E.: *Surg., Gynec. & Obst.* 70: 996-1005, 1940.
 Jensen, R. M., and McDonald, J. R.: *AM. J. OBST. & GYNEC.* 41: 268-274, 1941.
 Hamilton, V. C.: *AM. J. OBST. & GYNEC.* 42: 477-483, 1941.
 Foster, F. P.: *S. Clin. North America* 21: 917-936, 1941.
 Meaker, S. R.: *Proc. Am. Cong. Obst. & Gynec.* (1939) 1: 128-134, 1941.
 Gray, L. A.: *AM. J. OBST. & GYNEC.* 43: 387-400, 1942.
 Rubin, I. C.: *Bull. New York Acad. Med.* 18: 537-550, 1942.

Discussion

DR. I. C. RUBIN, New York, N. Y.—A number of interesting phases of sterility and infertility, which have become increasingly appreciated by gynecologists and the general profession in the past 25 years, have been presented in this paper. Some of the observations and conclusions, however, are at variance with the experience of other workers in this field and are therefore noteworthy. For example, a very small percentage of male infertility was encountered. Only 2 out of the 71 husbands were regarded as infertile according to the urologist's estimate of the seminal contents. The criteria of what constitutes normal semen vary considerably. Some are content to call many specimens normal, while others might regard the same specimens inadequate.

Despite Hühner's important contribution made over thirty years ago, and much work that has since been done by Moench and others on the morphological types of spermatozoa, there is as yet no unanimity of opinion as to the percentage of abnormal sperm compatible with fertility. The Hühner test has proved itself to

be a simple clinical method which enables us to ascertain the reaction between spermatozoa and the female genital secretions at their first encounter and incidentally determines the mechanical potency of the husband as well as his ability to produce spermatozoa.

The examination of the condom or unmixed specimen of semen is not entirely conclusive. It should be preceded or at least followed by the Hühner test which affords a truer estimate of the fitness of the spermatozoa. Their essential viability and virility are roughly estimated by their survival in the vaginal and cervical secretions, the only other natural environment they are destined to live in after being discharged from their source.

Even the finding of an adequate number of viable sperm in the vagina and cervix does not wholly exonerate the husband from the cause of the sterility, as Hühner and many of us at first believed. In the final analysis, the only real test of the fitness of the male gametes is their power to impregnate an ovum which eventually develops into a healthy living baby. Our results in combating childlessness may be expected to improve the more we are prepared to investigate the causes of the infertile mating rather than the infertile individual, devoting as much attention to the male as to the female partner.

It is only possible for me within the limited time allowed for discussion of this many faceted problem to take up one or two other essential points brought out in the paper. The endometrial biopsy gives information concerning a single menstrual cycle, but this does not necessarily hold for other cycles. I hesitate to take an endometrial specimen just before the onset of the menses for fear of interfering with a possible early pregnancy in a group of women to whom a single conception is precious.

The cases with hysterosalpingography and tubal insufflation in the series are, as Dr. Nicodemus has stated, too small in number to permit of broad deductions. It is quite possible that the percentage of pregnancies with respect to each method might be appreciably changed in a larger group. In my own series this has been found to be so.

The clinical diagnosis of hypothyroidism in connection with the basal metabolic rate has brought the most successful results in the series just reported. The rather large proportion of patients with hypothyroidism, as reported today, suggests differences in the subgroups met by others, which may account for the difference in therapeutic results. Chance and coincidence, even geographic location, play a not insignificant part in any analysis of therapeutic results, especially in sterility.

The fact that only 4 became pregnant of the 24 patients who were classified by the authors as normal from the endocrinologic point is difficult to explain, because 85 per cent of marriages in the general population prove fertile. Detailed analysis of all ascertainable factors might account for this fortuitous group. But it illustrates what a complex problem human sterility and infertility is despite the progress which has been made in our time. There still remains a relatively large group of sterile matings, with and without recognizable deficiencies, which defy all our efforts to relieve.

DR. KARL M. WILSON, Rochester, N. Y.—I would like to enlarge a little on the problem of determining the time of ovulation, particularly in those women who present a somewhat irregular cycle. In my clinic at the Strong Memorial, we have been devoting considerable attention to this angle of the problem in the last few years. When one has to deal with an irregular cycle, unless endometrial biopsy be taken at a particularly fortunate time, whether ovulation occurs, or when it occurs cannot be satisfactorily determined. There are a number of possible observations however, of which none is absolutely conclusive alone, but which taken together may prove of value in determining this point. These include the slight spotting which may occasionally be observed at the time of

ovulation if careful watch is kept; a rise in estrogenic hormone in the blood, which, of course, would require numerous and repeated observations; an increase in the pregnandiol excretion which may be taken as an indication of an active corpus luteum; also the vaginal smears, which, as emphasized by Traut, show an increase in leucocytes and cornified cells, less mucus and possibly erythrocytes at the approximate time of ovulation. Seguy and his collaborators have found an increase in the glairy cervical secretion in the midinterval of normal women followed by desquamation. Lamar has further shown that cervical mucus is under these conditions permeable to spermatozoa but not at other times. If temperature readings are carefully and accurately made throughout the cycle there is a sharp rise of about 0.3 of a degree F. just before or after ovulation. A rise of 0.3 in the pH of the vaginal secretion has also been noted at the approximate time of ovulation.

All these findings are of course only approximations but taken together they may be helpful in those who present irregular cycles and in whom it is therefore difficult to determine whether ovulation does occur at all, or if it does occur at just what time. Having obtained this information, an endometrial biopsy at the selected time will give us the final information.

DR. BENJAMIN P. WATSON, New York, N. Y.—Emphasis should be put upon the low basal metabolic rate in many of these sterility cases. We ought in particular to be careful about the dosage of thyroid. One so often finds a patient who comes in with a definite history of a low basal metabolic rate and discovers that she has been getting a half grain of thyroid a day. If there is a low basal metabolic rate, adequate doses of thyroid should be given and adjusted in accordance with further basal metabolic rate determinations. Most of these patients can take as much as three or four, or even five, grains of thyroid a day before any result is seen. Furthermore, we should pay as much attention to the basal rate of the husband as of the wife. It is my practice to give the husband the same therapy as the wife if his basal metabolic rate is low.

DR. J. C. LITZENBERG, Minneapolis, Minn.—I am certainly gratified to find that my results reported in 1937 still pertain, and that a low basal metabolic rate is an indication of hypothyroidism and also hypo-ovarianism, and is a frequent cause of sterility.

DR. ROBERT D. MUSSEY, Rochester, Minn.—The dosage of the different preparations of desiccated thyroid varies. For example, the Burroughs Wellcome product, an excellent preparation, has about one-fifth the strength per grain of the standard products, such as that of Parke, Davis' or Armour's. Often when a paper is discussed it is simply stated that 3 to 5 grains a day are given, while in another a dose of 1½ grains per day is mentioned. We must take into consideration the thyroid product which is being used.

DR. JEAN PAUL PRATT, Detroit, Mich.—Proof that the tubes are closed is sometimes difficult. I am sure we have all had experience with patients becoming pregnant after salpingography showed that the tubes were closed as in one instance noted by Dr. Nicodemus. On the other hand, I have come to feel that the results of the test for the patency of the tubes from above are more or less final. Nevertheless, a patient of mine married nine years had the patency of the tubes tested and at the same time an attempt was made to run salt solution through them. Some five years after that attempt, the patient did become pregnant.

DR. NICODEMUS (closing).—Dr. Rubin's point is well taken about the high incidence of normal sperm in the males. We questioned it very much ourselves and discussed it at length with our very competent urologist. The urologist states that he does the sperm count very accurately and he was not willing to change his mind about the fertility of these husbands.

THE MANAGEMENT OF ABRUPTIO PLACENTAE*

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AT THE present time there is much controversy among obstetricians as to the ideal treatment of abruptio placentae. Holmes¹ and Bartholomew² have always been opposed to routine cesarean section. The modified Rotunda treatment was introduced to American obstetricians by Polak,³ Irving,⁴ and Heffernan.⁵ The opposite view was given in a paper by Miller⁶ before this Society in 1941. Falls⁷ also favors immediate cesarean section in the severe cases. In a series of 88 severe cases, Cosgrove and Conway⁸ reported a maternal mortality of 4 per cent in those having sections and of 5.26 per cent in those who did not have sections.

The ever increasing number of hospitals with blood and plasma banks should markedly lower mortality from this condition regardless of whether treatment is radical or conservative. Reports of good results of the modified Rotunda method do not mean that these cases should be or can be treated in the home. The ideal place is in the modern maternity unit with an available blood or plasma bank.

In considering the treatment of all degrees of abruptio, it is apparent that individualization is necessary. Much depends upon the severity of the symptoms, parity of the patient, condition of the cervix, whether or not the baby is alive or jeopardized by asphyxia, and whether or not the patient is in labor. It seems better to classify cases according to the severity of maternal symptoms rather than to attempt a pathological classification, which is impossible to demonstrate at the time treatment must be inaugurated. I have studied the cases of abruptio placentae occurring in the last ten years at the Coleman Hospital and the Indianapolis City Hospital. (Fig. 1.) These have been divided into mild, moderate, and severe as has been suggested by McCord⁹ and others. The 30 cases occurring at the Coleman Hospital and the 24 at City Hospital are the basis for this paper. At the City Hospital, there were 24 abruptio placentae in 7,497 deliveries, and at Coleman, there was 30 cases in 10,705 deliveries, or a total of 54 in 18,202 cases, or an incidence of one in 337 cases. The incidence of severe cases was one in 2,250.

The Mild Cases

The degree of abruptio may range from a small separation as evidenced by a small clot on the maternal placental surface to the com-

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plete abruptio causing death of the fetus. Some cases of complete abruptio may produce no maternal symptoms. We may have a toxic patient, whom we have attempted to carry to viability, report loss of fetal movements without any other signs or symptoms of placental separation. At delivery, one may find that she has had a complete separation. These cases I have classified as mild. Also included are those

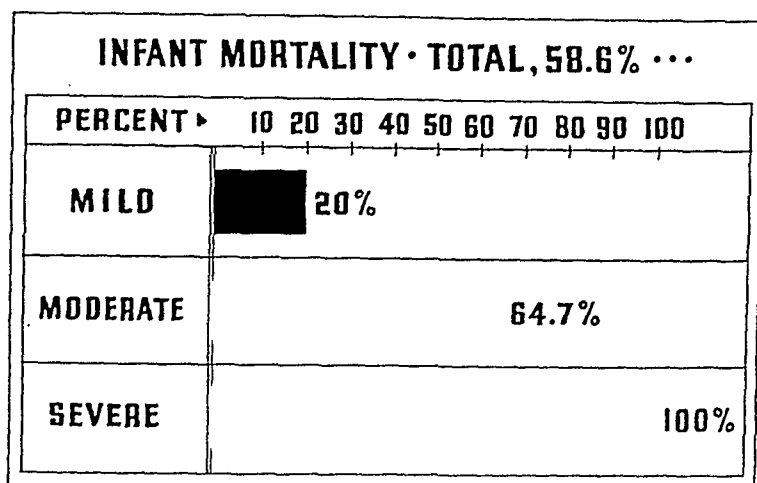


Fig. 1.

cases of slightly increased bleeding during labor with little or no change in fetal heart and requiring no particular treatment. Usually if there is slight separation, labor is so augmented that it is terminated in a short time. These cases then are for the most part cases where the diagnosis is obscure until actual delivery has been completed.

TABLE I. MILD GROUP

CAUSE		TYPE OF DELIVERY	
Toxemia	3	Breech extraction	2
Syphilis	1	Low forceps	4
Trauma	1	Spontaneous	9
Separated during breech extraction	1		
FETAL MORTALITY			
Total cases	15	Stillbirths	2
		Neonatal	1
PARITY OF PATIENT		PERIOD OF GESTATION	
Par i	6	7 months	1
Para ii	1	7½ months	2
Para iii	1	8 months	1
Para iv	3	8½ months	1
Para v	2	Term	10
Para vi	2		

In one of my patients, a 40-year-old patient with her first pregnancy, fetal heart tones and movements disappeared about two weeks before term. There was no evidence of toxemia. At the time of delivery, the placenta was found completely sheared from its attachment to the uterus by the presence of white infarcts completely covering the maternal surface. Two years later with a second pregnancy, I did a

cesarean section about 3 weeks from term in the hope of forestalling a similar incident. This time a live baby was obtained, but the placenta showed no tendency to infarct formation.

In this group of 15 mild cases, trauma was responsible for one, syphilis was present in another, toxemia in three, while in the others there was no demonstrable cause except that one placenta separated during a breech extraction.

Only one patient required transfusion. In one case the membranes were ruptured artificially. There were two breech extractions, four low forceps, and the remainder delivered spontaneously. Cesarean section was not used in any case.

Prematurity was present in one-third of the cases evidently caused by the abruptio. There were two stillborn babies and one neonatal death in the series of 15 cases.

In this group interference is almost always unnecessary, and the chief importance is the fetal loss due to prematurity and asphyxia, and the danger of a more severe type of abruptio developing.

The Moderate Cases

This group included those cases where a definite diagnosis could be made during labor. There was usually external bleeding, but shock was not present. In the majority of the patients, the fetal heart was still present. It is in this group where fetal salvage is often still possible. Fortunately, in many of the cases labor has started and is completed in a short time. Some of them will be first seen in the second stage of labor and, if the fetal heart is failing, can be terminated by low forceps. In the primipara just starting labor, cesarean section has its greatest use as the patient is in good condition and the baby can usually be saved. The administration of oxygen to the mother is very beneficial to a failing fetal heart while preparing for operation.

In the 19 cases of moderate severity at the Coleman Hospital, three cesarean sections were done and in each case living babies obtained. In the 12 cases at the City Hospital, sections were done on two patients with a salvage of one baby. Table II shows type of delivery and fetal salvage of the 31 cases of moderate severity. Toxemia was associated in 10 of the 31 cases. Twenty of the 31 were premature labors. Twelve cases required transfusions.

The Severe Cases

In this group, I have placed those patients entering the hospital in shock, with boardlike abdomens and no fetal heart tones. Also I have included one case not in shock, but with entirely concealed hemorrhage and who proved to have a Couvelaire uterus at operation. As this was the mildest of the severe cases clinically, all uteri in the group could be expected to show a comparable amount of damage.

TABLE II. THE MODERATE CASES

	COLEMAN HOSPITAL	CITY HOSPITAL	TOTAL
<i>Type of Delivery</i>			
Cesarean section	3	2	5
Spontaneous	(1 case with twins) 11	7	18
Breech extraction	(1 case with twins) 2	0	2
Breech extraction plus version and extraction	1 (twins)	0	1
Midforceps	1	1	2
Low forceps	1	1	2
Version and extraction	0	1	1
<i>Fetal Salvage</i>			
Total babies	22	12	34
Lived	9	3	12
Died	13	9	22
No fetal heart tone on admission	4	6	10
(Infant Mortality—64.7)			
Artificial rupture of bag of waters	5	0	5
Bag induction	2	0	2
<i>Cause</i>			
Toxemia	7	3	10
Syphilis	0	2	2
<i>Period of Gestation</i>			
7 months	2	4	6
7½ months	4	0	4
8 months	3	4	7
8½ months	1	2	3
Term	9	2	11
<i>Parity</i>			
Para i	10	2	12
Para ii	3	1	4
Para iii	2	0	2
Para iv	2	1	3
Para v	0	2	2
Para vi	0	3	3
Para ix	1	0	1
Para xi	1	1	2
Para xii	0	1	1
Para xiii	0	1	1

These are the patients where the greatest difference of opinion exists as to proper treatment. As the attending staff physician decided the particular treatment of these cases, some have been treated radically and some conservatively, while in one case at the Coleman Hospital, treated under my supervision, treatment was combined.

Unlike many cases of complete rupture of the uterus, when blood is lost faster than it can be given, it is possible to get the majority of cases of severe abruptio into better condition by preoperative transfusion. Therefore, there can be but little argument against waiting until that is done. Instead of procrastination while preparations are being made for transfusion, inauguration of conservative treatment may be attempted in those patients not in labor. The bag of waters

may be ruptured easily in the patient's own bed. I personally prefer not to use a cervical vaginal pack or the bag, and have had no experience with Willett's forceps. A Spanish windlass should be applied and wound tightly, and I believe does better than any type of abdominal binder. A one-minim dose of pituitrin should be given with a tuberculin syringe every half hour for two or three doses.



Fig. 2.—The uterus in the case treated by the combined method.

The question now is (1) whether the uterus can be stimulated to rhythmic contractions so that the baby may be expelled and if so, (2) whether or not the activity of the uterus will be sufficient to control hemorrhage in the early postpartum phase. The obstetrician or a trained resident must constantly observe the patient.

If it is clear that the patient is losing ground in spite of transfusion, as evidenced by frequent blood pressure readings and the character of the pulse, then more blood should be given and cesarean section done. Polak recognized this possibility and one of his 16 patients was so treated. On the other hand, it is remarkable how, in many cases the uterus can be stimulated and active progressive labor will be started. Anyone who has not attempted this method of treatment will be impressed by its advantages, if he will only give it a trial. In some cases the labor will be short, terminate spontaneously, postpartum uterine activity will be satisfactory and after the first 24 hours, the patient

will progress as a normal patient to be discharged much sooner than if she had been operated upon.

In 34 patients treated conservatively, Irving had only one case where the uterus would not expel its contents. Also, he has not seen a case where uterine activity would not control postpartum bleeding. However, O'Regan¹⁰ recently reported 2 deaths from this at the New York



Fig. 3.—Microscopic section showing gross infiltration of the blood and separation of muscle fibers.

Lying-in Hospital. One patient at the Coleman Hospital was saved by blood and hysterectomy. Though the baby was delivered by low forceps after conservative treatment, bleeding continued very profusely after expression of the placenta. The uterus was packed and bleeding continued through the packing, necessitating a hysterectomy. It has been stated that a change from conservative to radical treatment is an obstetrical blunder, but to have persisted with conservative treatment here would have meant disaster. The uterus in this case is shown in Fig. 2, and I believe most of you would term it a typical Couvelaire uterus though not to the degree of many. The appearance of the uterus is not necessarily a good criterion as to its ability to contract. A short time after this case, at St. Vincent's Hospital, I did a cesarean upon a patient with her first pregnancy with partial abruptio, but with fetal heart tones still present. Her uterus was very similar in

appearance to this one, but responded nicely after extraction of the placenta and was not removed. Occasionally, in a uterus left at cesarean section, another operation for its removal may be necessary as illustrated in Frank's¹¹ case. If one does cesarean section on these cases and removes all uteri that show hemorrhage under the serosa and in the region of the great vessels, then many uteri will be sacrificed unnecessarily. I have seen similar petechiae and subserosal hemorrhages in one case of obstructed labor not associated with abruptio, and in another case with marked dextral rotation of the uterus.

Following are eight short reports on the severe cases of abruptio in this series. Another severe case of abruptio, seen in consultation at the Methodist Hospital, was successfully treated by rupture of the membranes, Spanish windlass, and pituitrin.

Severe Cases Treated by Immediate Cesarean Section

CASE 1.—Mrs. M. B., #3701, aged 37, para xi, with history of syphilis, entered City Hospital August 2, 1937, from outdoor service at 8 months' gestation. There were external bleeding and shock. The abdomen was tense, boardlike, and continuous pain was present. The fetus could not be palpated, and there were no fetal heart tones. Blood pressure was 45/0. The patient was not in labor. She was given a 500 c.c. blood transfusion (hemoglobin #6, 33 per cent and red count 1,600,000), and a cesarean section was done. The placenta was completely separated and the uterus was full of dark clots. Another transfusion was given on the second postoperative day. The patient was discharged on the twenty-second postpartum day. She has had three deliveries from below since.

CASE 2.—Mrs. G. D., C-8 841, aged 20, nullipara, a congenital syphilitic, had been receiving antisyphilitic treatment. She was admitted to the Coleman Hospital October 9, 1935, for treatment of toxemia at about 7 months' gestation. She had a fulminating toxemia, urine was loaded with albumin and casts, and there was blurring of vision. She was scheduled for cesarean section and sterilization on October 11. The previous evening, the patient developed sudden pain, started to bleed profusely, her blood pressure dropped from 174/120 to 110/65. She went into shock and the fetal heart disappeared. She was given a transfusion and cesarean section done. Placenta was entirely separated and a stillborn fetus delivered. Hysterectomy was also done, and the patient was discharged on the sixteenth postoperative day.

CASE 3.—Mrs. E. H., XC-24 504, aged 24, nullipara, and a private patient of one of the staff, had been in Coleman Hospital from August 27, 1938, to September 3, 1938, for treatment of a toxemia. She had greatly improved although showing about 0.4 gram per liter of albumin and blood pressure had returned to normal. On September 17, 1938, she was readmitted to the hospital with a very hard boardlike abdomen and in continuous pain. There was no external bleeding. Fetal heart tones were absent. She was operated on shortly after admission, and a stillborn baby at term was removed. Placenta was adherent to top of fundus, attached only around circumference. Between placenta and uterus was a mass of blood clot and free blood totaling about 1,500

cubic centimeters. There was much gross extravasation of blood into uterine wall and the uterus was copper in color. Uterus was removed. Transfusion was given during operation and later two more transfusions were given. Patient was discharged on the twentieth postpartum day.

Severe Cases Treated Conservatively

CASE 1.—Mrs. E. P., 50 585, aged 35, a para v, at 8 months, was admitted to City Hospital at 9:30 A.M., November 6, 1941. She was in definite shock and in labor. Her skin was cold and clammy, and her pulse fast and thready. There were no fetal heart tones. Blood pressure was 40/0. Abdomen was boardlike, and there was some external bleeding. Sequence of events were: admitted at 9:30 A.M.; at 10:00 A.M. she received 500 c.c. blood plasma and 500 c.c. N.S.; vaginal packing was done and 500 c.c. blood given. She also received morphine sulfate, gr. $\frac{1}{4}$. At 2:30 P.M. she was repacked and at 4:15 delivered a stillborn boy. Another 500 c.c. of blood were given after delivery and was repeated on Nov. 7, 1941. She was discharged on the tenth postpartum day.

CASE 2.—Mrs. D. J., 109176, aged 30, a para v and 7 months pregnant, had a history of nephritis. She was admitted to the City Hospital on my service at 10:15 P.M., September 30, 1940. She was not in labor, but was in profound shock. Skin was cold and clammy. Blood pressure 90/40. Abdomen was boardlike and there was acute abdominal pain, especially on one side. Some external bleeding was present. The red count was 1,700,000 and hemoglobin, 39 per cent. Sequence of treatment was as follows: admitted 10:15 P.M. Spanish windlass was applied, bag of waters ruptured artificially and one minim of pituitrin given. At 11:00 P.M. she was given 1,000 c.c. of 5 per cent glucose in sterile water. At 11:30 morphine sulfate, gr. $\frac{1}{6}$. At 1:00 A.M. 500 c.c. of blood. At 3:00 A.M. morphine sulfate, gr. $\frac{1}{6}$. At 9:25 A.M. 500 c.c. blood. At 4:40 P.M. spontaneous breech delivery of a stillborn male. At 4:50 P.M. breech extraction of a stillborn female. On October 2, she received 500 c.c. blood and again on October 10. She was discharged on the twelfth postpartum day.

CASE 3.—Mrs. L. F., aged 26, nullipara, C-11 102, with toxemia, was admitted to the Coleman Hospital at 9:00 P.M., August 12, 1936, in labor and in shock with extreme pallor. Blood pressure 100/80, some external bleeding, uterus tonically contracted and no fetal heart tones present. At 10:00 P.M. intravenous of 1,000 c.c. 10 per cent glucose in sterile water. At 12:15 A.M. 500 c.c. transfusion. At 3:45 A.M. intravenous of 1,000 c.c. glucose in distilled water and also sodium amytal, gr. VISS. At 4:00 A.M. she delivered spontaneously at which time her blood pressure was 200/136. The stillborn girl was near term. The mother was discharged on the fourteenth postpartum day.

CASE 4.—Mrs. B. D., 205 242, aged 36, para vii, was admitted to City Hospital on August 13, 1942, at 2:00 A.M. She was in labor and in shock. Her skin was cold and clammy, uterus boardlike, blood pressure 72/10. No fetal heart tones were present and there was some external bleeding. Sequence is as follows: admitted 2:00 A.M. At 2:25 A.M. given 500 c.c. plasma. At 3:27 A.M. spontaneous delivery of a stillborn girl and uterus packed. At 5:00 A.M. given 500 c.c. blood, repeated on August 14. The patient was discharged on the tenth postpartum day.

Severe Case With Combined Treatment

Mrs. R. B., XC-48 051, a secundipara at term, was admitted to my service at Coleman Hospital at 1:30 P.M., January 31, 1943. She was bleeding profusely, had severe abdominal pain, but was not in labor. She was in shock with cold, clammy skin and thready pulse. Blood pressure was 100/60 and fetal heart tones were absent. Upon admittance, she was given morphine sulfate, gr. $\frac{1}{6}$. At 1:30 P.M. she received 500 c.c. plasma and 500 c.c. blood. Bag of waters was ruptured artificially. At 2:00 P.M. a Spanish windlass was applied and one minim pituitrin given. At 6:15 P.M. she was delivered of a stillborn girl by low forceps and the placenta expressed followed by about 800 c.c. of blood and clots. Five hundred c.c. plasma, 500 c.c. blood, 500 c.c. normal saline with glucose, ergotrate intramuscularly and intravenously were administered. Uterus packed. At 8:00 P.M. she was given 500 c.c. of plasma. At 10:30 P.M. 500 c.c. blood started and hysterectomy done (typical Couvelaire uterus). A total of 2,000 c.c. whole blood and 1,500 c.c. plasma were administered. Mother was discharged on fourteenth postoperative day. Without blood and a change to radical management, this patient could not have been saved.

Summary

The 54 cases of abruptio placentae occurring in 18,202 deliveries have been studied. In the 15 cases of the mild group, interference was almost always unnecessary and their chief importance was the fetal loss due to prematurity and asphyxia.

In the 31 cases of moderate severity with 34 babies, the fetal mortality was 64.7 per cent. Five cesarean sections were done, the remainder being delivered through the normal passages.

Of the eight severe cases, three were treated by immediate cesarean section, four were successfully treated by conservative treatment and one was saved by combined treatment. All babies were dead when treatment was started.

There was no maternal mortality in the total series. Total fetal mortality was 58.6 per cent.

Conclusions

1. The availability of blood and plasma is imperative in the treatment of moderate and severe cases of abruptio placentae.

2. The ideal place for cesarean section is in the abruptio of moderate degree with the patient not in labor or with labor not advanced, and fetal heart tones present.

3. For the severe cases, conservative treatment is in many instances ideal, but not all cases can be thus treated successfully.

4. A trial with conservative treatment in the severe group is favored. An occasional patient will require termination by cesarean section, with or without hysterectomy. In the cases expelling their babies through the normal passages, an occasional patient will require hysterectomy because of postpartum bleeding. Combined treatment should play a definite role in the management of abruptio placentae.

References

1. Holmes, R. W.: *Am. J. Surg.* 48: 61, 1940.
2. Bartholomew, R. A.: *AM. J. OBST. & GYNEC.* 18: 818, 1929.
3. Polak, J. O.: *AM. J. OBST. & GYNEC.* 21: 218, 1931.
4. Irving, F. C.: *AM. J. OBST. & GYNEC.* 34: 881, 1937.
5. Heffernan, R.: *New England J. Med.* 214: 370, 1936.
6. Miller, J. R.: *AM. J. OBST. & GYNEC.* 42: 754, 1941.
7. Falls, F. H.: *Lancet* 54: 107, 1934.
8. Cosgrove, S. A., and Conway, D. F.: *J. Missouri M. A.* 38: 334, 1941.
9. McCord, J. R.: Discussion of Miller's paper, q.v.
10. O'Regan, J. A.: *AM. J. OBST. & GYNEC.* 46: 566, 1943.
11. Frank, C. W.: *AM. J. OBST. & GYNEC.* 33: 512, 1937.

Discussion

DR. SAMUEL A. COSGROVE, Jersey City, N. J.—Dr. Gustafson presents a thoughtful analysis of 54 consecutive cases of abruptio of varying degree, managed by different methods, over a ten-year period, without maternal loss. It is doubtful if this splendid record can be generally maintained. Our own last 51 cases also showed no maternal mortality. But in larger series, it is inevitable that there will be some maternal loss due to concomitant factors. In three of the four maternal deaths reported by Conway and myself in 1941, severe toxemia was the sole or importantly contributory cause of death.

I thoroughly concur with the essayist in the following points: (1) The importance of modern resources for blood replacement in successful management; (2) the necessity for classifying and individualizing cases; (3) the validity of the seriousness of maternal symptoms as a basis for classification and estimation of severity; (4) the general applicability of conservative treatment of those cases falling within Dr. Gustafson's mild group, and a large majority of his moderate group; (5) the importance of cesarean section for fetal salvage, and in anticipation of progress to more severe states, in some cases of his moderate group; (6) the extremely rare necessity for sacrifice of the uterus.

Classification of these cases is somewhat difficult. In our former report, we divided cases into only two groups, the mild and severe, in conformity with Dr. Gustafson's own proposal to base such classification on maternal symptomatology. Certainly on this basis some of the cases classified by him as moderate might be considered severe, even though not conforming to the very strict criteria for his severe group. Without such correspondence of classification, it is exceedingly difficult to compare accurately differences in management. However, in regard to those cases which Dr. Gustafson classes as severe, and many of his moderate group, we would be inclined, I think, to place somewhat stronger emphasis than he has on the propriety of radical measures, implemented, of course, by proper antishock treatment.

In our 51 recent cases, there were 38 classifiable as moderate, and 13 as severe, by Dr. Gustafson's scheme of classification. None were of his clinically negligible "mild" type. Of the 38 moderate cases there were:

Cesarean sections	16	42.1%
Delivery by other methods	22	57.9%
Maternal mortality	0	
Fetal mortality	4	10.5%

Of the 13 severe cases there were:

Cesarean sections	10	76.1%
Delivery by other methods	3	23.9%
Maternal mortality	0	
Fetal mortality	13	100.0%

Of the total there were:

Cesarean sections	26	51.0%
Delivery by other methods	25	49.0%
Maternal mortality	0	
Fetal mortality	17	33.3%

Thus, the broader application of radical methods to this group has been salutary to the mothers and appears to have resulted in the salvage of two-thirds of the infants as compared to a fetal loss in Dr. Gustafson's series of almost 60 per cent.

DR. LOUIS E. PHANEUF, Boston, Mass.—The service at the Carney Hospital is a combined one having an equal number of beds in gynecology and obstetrics. I have looked up the obstetric records during the seven years preceding January 1, 1944, and found that during this period of time, there had been 4,508 deliveries. Among these, there occurred 38 cases of abruptio placentae, an incidence of 0.84 per cent or 8.4 cases per 1,000 deliveries. These 38 cases were classified as severe in 9, moderate in 13 and mild in 16. The range in parity was from 0 to 8. The ages ranged from 23 to 46 years. Seven of the women had severe pre-eclampsia. The period of gestation varied between 20 weeks and 42 weeks.

The methods of delivery consisted in the following: in rupture of the membranes, cervicovaginal packing and spontaneous delivery in 21 patients; packing and forceps extraction in 3 patients; Voorhees' bag and spontaneous delivery in 2 patients; vaginal hysterotomy and breech extraction in 1 patient; embryotomy in 1 patient, and cesarean section in 10 patients.

In these 38 cases, 37 mothers recovered, and one died, a maternal mortality of 3 per cent. The mother who died was 23 years of age, a gravida 2, para 1, in the thirty-fifth week of her pregnancy. Her prenatal course had been uneventful until she suffered a fall two days before admission. One-half hour before admission, she began to bleed vaginally. She was not in labor, but bleeding profusely, and the fetal heart tones were good. She was delivered of a living child by cesarean section and was at once given fluids intravenously and 600 c.c. of blood. Her uterus contracted well, but two hours and a half after delivery she had a sudden, profuse hemorrhage from which she succumbed despite all the efforts to combat it. This woman's life might have been saved had a hysterectomy been done, but, at the time of delivery, there was no indication for doing it.

The fetal heart tones were not observed on admission in 14 patients, or 36 per cent. In the group of 38 infants, 16, or 42 per cent, survived. Five babies lived from 3 to 12 hours and 17 were stillborn, thus 22 infants, or 58 per cent, perished. Ten of these 22 dead babies, 45 per cent, were premature.

In regard to cesarean section in the severe cases accompanied by uterine apoplexy, the so-called Couvelaire uterus, I have made an observation which has some practical value. If the bladder is separated from the uterus, there is usually found an area in the lower uterine segment which is free from hemorrhagic changes. This area is of such size as to permit the placing of the transverse half-moon incision within it, but it is not large enough to allow a longitudinal incision without encroachment on that part of the uterus involved in the hemorrhagic process, namely, the corpus. A transverse incision within this zone will permit secure uterine closure, and will be frequently responsible for saving the uterus, whereas in the classical cesarean section, the incision being placed in the hemorrhagic corpus, hysterectomy frequently becomes necessary, because of the difficulty of closing such an incision in hemorrhagic and friable tissue.

THE TREATMENT OF URINARY INFECTIONS WITH SULFASUXIDINE (SUCCINYLSULFATHIAZOLE)*

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The Problem

URINARY infections are frequent and often serious complications of gynecological and obstetrical conditions. The etiological agent in the production of such infections may be any one of a variety of microorganisms, but in the majority of them some member of the coliform group of bacilli is the responsible agent. Of this group *Escherichia coli* is the most frequent offender. These facts are especially true with regard to those infections occurring during pregnancy and the puerperium.

By careful attention to eradication of such contributing factors as lesions productive of urinary stasis and distant foci of infection, much progress has been made in the prevention and treatment of these infections. The therapy of the infections, once established, has been greatly augmented by modern chemotherapeutic methods, especially the use of the sulfonamide drugs. Chemotherapy, however, has proved generally more effective in the acute forms of urinary infections than in the chronic varieties. So long as such complicating factors as stasis or calculus are permitted to exist, even the most efficient means of chemotherapy will usually fail to eradicate the infection. In some other cases, even though no such factors have existed, or if they have existed have been thoroughly eradicated, infection will persist in a chronic state in spite of the most efficient known methods of chemotherapy. In other cases, it is found that the infection will subside temporarily in response to chemotherapy, but will quickly recur after withdrawal of the drugs. Such chronic or frequently recurring infections generally result in slowly progressive damage to the kidneys, and furthermore, constitute an additional hazard, in that should such stasis-producing factors as the physiological dilatation of the renal pelvis and ureters occurring during pregnancy or postoperative or postpartum urinary retention intervene, acute febrile episodes of pyelonephritis are very apt to result. It is most important, therefore, that use be made of every available means to accomplish complete and permanent eradication of urinary infections of this type.

Urinary infection by all types of organisms is generally considered to be secondary, in that the organisms reach the urinary tract from

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some source elsewhere in the body. The possible routes by which access to the urinary organs is attained have for many years been the subject of much contention, and a vast literature has grown out of these discussions. The question is not entirely settled, and for the present discussion it is of no great importance. It has been thoroughly reviewed in most textbooks of urology as well as in many independent articles.

For coccal infections, elimination of the source depends upon a thorough search for, and eradication when found, of focal infections in distant parts of the body. In the case of coliform infections, however, the normal flora of the intestinal tract constitutes a permanent massive reservoir of the offending organisms. If this reservoir can in some way be depleted even temporarily, and the constant source of infection thus removed, the normally high resistance of the tissues of the urinary tract to infection may be given a change to recover, so that chronic infection may subside, and frequent recurrences will be less apt to occur in the future.

The Drug

Since about 1940, considerable investigation has been carried out in attempts to find a drug of the sulfonamide group locally effective in the intestinal tract. Such work is still in progress and has already met with considerable success. It is desirable that such a drug should be poorly absorbed from the intestine, so that it may remain to exert its effect upon the bacterial flora of the large bowel, and so that possible toxic effects resulting from its absorption into the blood stream may be reduced to a minimum. To date, the most efficient drug fulfilling these criteria is Succinylsulfathiazole, manufactured by Sharp and Dohme under the trade name of Sulfasuxidine, and first thoroughly studied both experimentally and clinically by Poth and his collaborators¹⁻⁴ in the surgical department of the Johns Hopkins University. The chief clinical uses of the drug so far reported are preparation of the bowel for operation upon it, the treatment of bacillary dysentery, and the treatment of ulcerative colitis. Although Poth's first preliminary report appeared in October, 1941,¹ already a considerable literature regarding the use of the drug for these purposes has appeared.

In dogs the drug was found to be nontoxic and harmless when administered in doses of 1 Gm. per kilogram of body weight daily for as long as five weeks. This dosage resulted in a fecal content of the drug of 5 to 10 per cent, and only about 5 per cent of the ingested drug was excreted in the urine. Crystalluria did not occur, and the observed blood levels were never more than 1.5 mg. per cent of sulfathiazole and 2 mg. per cent of succinylsulfathiazole. The dosage for human beings recommended by Poth and his associates was an initial dose of 0.25 Gm. per kilogram of body weight, and 0.25 Gm. per kilogram in six divided doses daily thereafter. With this dosage, the blood level of free sulfathiazole reported by Poth rarely exceeded 1.5 mg. per cent, although

occasionally, higher levels were found for one or two days during the administration of the drug. The highest level recorded was 2.9 mg. per cent, and this was for only one day. The average of 77 determinations in 10 human subjects was 0.95 mg. per cent. The blood levels of succinylsulfathiazole ranged from 0.5 to 8 mg. per cent, the average being 2.11 mg. per cent. In general, the higher blood levels of both substances were obtained on the earlier days of administration following the initial massive dose. The average daily urine excretion in the same cases was found to be 0.34 Gm. of free sulfathiazole and 0.38 Gm. of succinylsulfathiazole.

No toxic reactions to the drug were encountered in the earlier observations of Poth, but subsequently an occasional case with skin rash or febrile reaction has been reported. The subjects in whom these reactions occurred usually have been shown to be highly sensitive to sulfathiazole, as similar reactions were precipitated by single small doses of this drug.⁴⁻⁶ One case of fatal agranulocytosis following administration of the drug was reported by Johnson.⁵ Clay and Pickrell⁶ have reported the only case yet recorded of hematuria and crystalluria resulting from administration of the drug.

According to the work of Poth and his associates, the purpose accomplished by this drug is to reduce greatly the concentration of the intestinal bacterial flora, especially the coliform bacilli. It was found that when the suggested dosage was administered the count of *E. coli* in the stools was reduced in from one to seven days from the normal of 10,000,000 or more to less than 1,000 per Gm. of wet stool. In some cases after administration of the drug no *E. coli* could be grown in stool cultures. The drug has the additional effects of overcoming any tendency to constipation and of rendering the stools soft and odorless.

Methods and Results

It occurred to us that in this drug we might have an agent which would be effective therapeutically in the treatment of those cases of *E. coli* infection of the urinary tract which had proved refractory to other means of therapy. To test this supposition, the drug has been used in the treatment of 41 cases of urinary infection. In most of these 0.25 Gm. per kilogram of body weight daily in either four or six divided doses has been given for one week, and half this daily dose for from one to two additional weeks. In 34 of these patients the urine yielded *E. coli* in pure culture. In 17 of these, there was acute pyelitis either during pregnancy or the puerperium, and in the other 17 the infections were not immediately related to the pregnant state.

The character of the urinary infection, the results of previous treatment, and the immediate and remote response to treatment by succinylsulfathiazole, in these 34 patients are recorded in Table I. Disregarding the one patient with calculi in the left kidney in whom a bacteriologic

TABLE I. RESULTS OF TREATMENT WITH SULFASUXIDINE OF 34 CASES OF URINARY TRACT INFECTION IN WHICH PURE CULTURES OF *E. coli* WERE GROWN FROM THE URINE

DIAGNOSIS	CASES	PREVIOUS CHEMOTHERAPY		IMMEDIATE RESULT OF SULFASUXIDINE TREATMENT		LATE RESULTS		
		NO SUCCESS	SUCCESS TEMPORARY	SYMPTOMATIC CURE	BACTERIOLOGIC CURE	NO. FOLLOWED	SYMPTOMATIC CURE	BACTERIOLOGIC CURE
Pyelitis of pregnancy	9	3	—	9	7	9	8	8
Puerperal pyelitis	8	0	—	8	7	7	7	6
Chronic or recurring cystitis	5	—	3	5	5	5	4	3 + 1*
Acute cystitis	1	—	—	1	1	1	—	Recurrence 8 mos. with 2nd cure for 5 mos.
Chronic pyelitis	8	3	1	8	8	5	5	5
Acute pyelitis	2	—	—	2	2	0	—	—
Chronic pyelitis with renal calculi	1	—	—	1	0	—	—	—
Total	34	6	4	34	30	27	24	22

*This patient had always had severe symptoms associated with her recurring attacks of bladder infection. A year after treatment with sulfasuxidine, she reported from England by letter that she had suffered no recurrence of symptoms.

cure was not expected, in 30, or 91 per cent of the 33 patients, the urine was rendered sterile as a result of the treatment. The time required to accomplish this purpose in most of the successful cases was less than one week. Furthermore, in 23 of these patients who have been followed subsequently for from three to twenty months, there has been recurrence of infection in only 3.

Attention is called especially to the 10 cases shown in Table II, in whom previous chemotherapy had proved unsuccessful in so far as any permanent eradication of infection was concerned. It was to determine the effect upon this type of case that the study was originally undertaken, and although the group is small the results have been gratifying, for apparently we have been able to demonstrate in this drug an effective therapeutic agent for a type of case intractable to all previous methods of treatment.

TABLE II. RESULTS OF SULFASUXIDINE THERAPY IN 10 PATIENTS WHO PREVIOUSLY HAD BEEN TREATED UNSUCCESSFULLY OR WITH ONLY BRIEF TEMPORARY SUCCESS WITH OTHER SULFONAMIDES, AMMONIUM MANDELATE, OR BOTH

IMMEDIATE RESULTS		ULTIMATE RESULTS		
SYMPTOMATIC CURE	BACTERIOLOGIC CURE	NO. FOLLOWED	SYMPTOMATIC CURE	BACTERIOLOGIC CURE
10	9	8 2 too recent	8	6

Three of the obstetric patients had been treated previously unsuccessfully with sulfathiazole, one in a previous pregnancy and two in the same pregnancy in which the sulfasuxidine proved successful. Of the nonobstetric group, seven had been treated unsuccessfully with other drugs. In two of these sulfathiazole had been used, in one of them twice, and in a third sulfathiazole, sulfadiazine, and ammonium mandelate had all failed. In four others either sulfadiazine, ammonium mandelate or both had been used with immediate success but had not prevented rapid recurrence of the infection. A few brief case reports will serve better than statistics to emphasize the value of the drug in cases of this type.

CASE 1.—F. L., white, single, aged 58, had suffered an attack of acute left pyelitis in 1938. There had been a febrile course with chills lasting five weeks. Following recovery from this, intravenous pyelography had shown normal excretion of the dye and normal upper urinary tracts. Subsequent to that, she had suffered from attacks of acute cystitis about once each year, each attack lasting about one week, and responding symptomatically to ammonium mandelate administered under the direction of her family physician. She had for years suffered from severe chronic constipation.

She was seen first by one of us (H.S.E.) on July 22, 1942, having just recovered from such an attack of cystitis for which ammonium mandelate had been used. The catheterized urine was microscopically negative, but the culture yielded a heavy growth of *E. coli*. Three days later, July 27, there was recurrence of acute symptoms with massive

pyuria, and again a heavy growth of *E. coli* was obtained. The patient was hospitalized, and 4 Gm. of sulfadiazine were given daily for six days. The symptoms and pyuria cleared rapidly, but the culture was still positive on July 31. On April 6, 1943, there was another flare-up of cystitis with pyuria and *E. coli* bacilluria. Sulfasuxidine 3 Gm. four times daily was begun at once, and continued for one week, and 1.5 Gm. four times daily were given for two additional weeks. On April 13, at the end of the first week, the urine was sterile, the symptoms had subsided, and the patient reported great relief from her chronic state of constipation. There has been no recurrence of symptoms up until the present, and urine cultures obtained on April 20, May 4, June 22, and September 21, 1943, and January 31, and May 27, 1944, have all been sterile.

CASE 2.—R. R., colored, aged 46, was admitted to the gynecological service on August 25, 1941, with acute right-sided pyelonephritis resulting from obstruction of the ureteropelvic junction by a calculus. *E. coli* was grown in pure culture from the urine. The acute symptoms were relieved by nephrostomy and sulfathiazole. On December 30, 1941, cystoscopic study revealed *E. coli* in both the bladder and left kidney urines, and a calculus in the right kidney. The left pyeloureterogram was normal. In march, 1942, she was readmitted and on March 30, the calculus was removed from the right kidney, the lower pole of the kidney was resected, and an incisional hernia which had resulted from the nephrostomy was repaired. Postoperatively she was again given sulfathiazole, but subsequently repeated cultures from the bladder and both kidneys continued to show *E. coli*. On December 2, 1942, sulfasuxidine therapy was started, and a full three-week course was given. After one week of the drug, the bladder culture showed only a light growth of *Staphylococcus albus*, and cultures taken September 23, 1943, January 6, 1944, and June 7, 1944, were all sterile. There has been no recurrence of urologic symptoms.

CASE 3.—T. F., white, aged 19, was delivered June 10, 1942, by classical cesarean section because of severe pre-eclamptic toxemia. The postoperative course was complicated by severe bilateral pyelonephritis, the culture showing *E. coli*. After nine days of sulfathiazole therapy, urine culture still yielded a heavy growth of the organisms. The patient was discharged on June 28, 1942, and readmitted July 2, 1942, with recurrent acute symptoms and a very large tender left kidney. The fever subsided after four days of sulfadiazine, and on the sixth day the urine was reported as sterile, but still contained much pus. On the third admission, July 21, 1942, she again had acute left pyelonephritis with urine showing much pus and a heavy growth of *E. coli*. She was transferred to the gynecologic service where urologic studies showed a left hydronephrosis with obstruction at the ureteropelvic junction. The half hour phenolsulfonphthalein excretion was 10 per cent from the left and 8 per cent from the right kidney.

Ammonium mandelate was given for a week, but the patient continued extremely ill with fever and left flank pain, and on August 8, 1942, the left kidney was explored and removed. The kidney was very large and contained many small cysts suggesting polycystic disease. Many of these were filled with pus, and there was generalized acute pyelonephritis. Ten days after operation, the urine still showed clumps of pus cells and a heavy growth of *E. coli*.

The patient was readmitted September 23, 1942, with recurrent right pyelonephritis due to *E. coli*, and mild uremia. Sulfasuxidine was given for two weeks, the temperature was normal by the sixth day, and the urine from the right kidney was sterile before discharge. There has been no recurrence of acute symptoms. May 31, 1943, the blood nonprotein nitrogen was 53 mg. per cent, the two-hour phenolsulphthalein excretion was 25 per cent, and culture of the bladder urine yielded *Staphylococcus aureus*. On March 31, 1943, the urine was sterile, and on January 25, 1944, showed *Staphylococcus albus* and *alpha streptococci*. The last culture obtained on May 18, 1944, was sterile.

CASE 4.—A. B., colored, aged 61, was treated for acute pyelitis and cystitis due to *E. coli* with sulfathiazole for six days beginning April 4, 1943. Culture was sterile on the fourth day of treatment, but was positive again after one month. Urologic studies showed a half hour 'phthalein excretion of 15 and 10 per cent from the right and left kidneys, respectively. The left pyelogram was normal and on the right there was ptosis, hydronephrosis, and hydroureter. Symptoms of acute cystitis and left pyelitis recurred on October 7, 1943. After two weeks of sulfasuxidine, the urine was sterile and microscopically negative. Repeat cultures and specimens six and nine months later, March and June, 1944, were also negative.

CASE 5.—A. M., white, aged 22, was seen first February 10, 1938, at the seventh month of her first pregnancy, having had symptoms of right pyelitis since late December. She had been treated ineffectively with sulfathiazole, which had been tolerated poorly and had caused severe nausea and vomiting. She was running low-grade fever, and the urine contained much pus and showed a heavy growth of *E. coli*. Strangely, she tolerated ammonium mandelate well and was kept afebrile until term by almost continuous use of this drug. The cultures remained positive, however, and whenever the drug was omitted the fever recurred.

After delivery the fever and symptoms subsided. On April 3, 1939, appendectomy was performed for acute appendicitis. Intravenous pyelograms made during convalescence showed normal kidneys and ureters. The bladder culture showed *E. coli*, but the kidney cultures were sterile. Ammonium mandelate was again given, and bladder cultures obtained on June 12, and August 14, were sterile.

A second pregnancy was uncomplicated, and the patient was delivered in November, 1941. She was next seen on January 16, 1943, four and a half months' pregnant with symptoms of mild acute right pyelitis. The urine contained pus, and the culture showed *E. coli*. On January 22, six days after beginning sulfasuxidine, there were no symptoms, and the urine was negative microscopically and on culture. There were no further complications during the pregnancy, but when the patient returned by request on February 28, 1944, the urine showed *E. coli* bacilluria but only an occasional pus cell. Treatment with sulfathiazidine 0.1 Gm. per kilogram daily was instituted, and cultures obtained on March 13 and 27, and May 29 were sterile.

CASE 6.—J. B., colored, aged 16, was admitted to the obstetric service on November 2, 1943, at the seventh month of pregnancy, with acute bilateral pyelitis probably of three weeks' duration. The culture yielded

a heavy growth of *E. coli*, and on November 4, sulfathiazole therapy was started with an initial dose of 4 Gm. followed by 1 Gm. every four hours. The patient improved rapidly, and was afebrile by the third day of treatment, but the hemoglobin decreased from 64 to 48 per cent, so the drug was stopped, and a transfusion of 500 c.c. of citrated blood was given. On November 11, she was discharged free from symptoms but the urine still showed 10 pus cells per high power field, and a culture was not obtained. A culture obtained on November 22 was reported as sterile, although the urine contained much pus and the patient was suffering from symptoms of acute cystitis. She was readmitted with recurrent acute pyelitis on December 2, 1943. Sulfasuxidine was started on the day of admission, and all symptoms had subsided by the fourth day, December 5. On December 7, however, there was still much pus in the urine, and the culture was positive. She received 12 Gm. of the drug daily for the first week, and 6 Gm. daily for two additional weeks. She was delivered uneventfully at term on December 28, 1943. Cultures obtained on December 16, December 23, January 1, and February 16 were all sterile. Intravenous pyelograms on January 4 showed normal tracts for the first week post partum.

CASE 7.—R. S. had had a known persistent *E. coli* infection since a hysterotomy in 1934, at the seventh month of pregnancy because of acute pyelitis. There was an acute exacerbation in 1942, treated without specific chemotherapy. She is now pregnant at the date of writing, with the expected date of delivery July 6, 1944. Cultures on December 9, 1943, and January 8, 1944, showed heavy growths of *E. coli*. Sulfasuxidine therapy was begun on the latter date and continued until February 1. On January 18, 1944, the urine culture was sterile and has remained so since. There is a residual urine of about 100 c.c. because of a neurogenic bladder resulting from an old postmeningitic paraplegia.

CASE 8.—C. P., white, aged 39, had had nine pregnancies with only two living children. For seventeen years she had had right flank pain with radiation along the course of the ureter, and recurring pyelitis with each pregnancy. Urologic investigation revealed half hour 'phthalein excretion of 20 per cent from the right and 10 per cent from the left kidney. There was a dense stricture of the left lower ureter with hydroureteronephrosis. The left kidney was removed on June 8, 1942, and showed hydronephrosis and chronic pyelonephritis. Culture from the right kidney just before operation showed *E. coli*. Following the left nephrectomy, the right side was treated by repeated ureteral dilations and showed cultures consistently positive for *E. coli*. Sulfasuxidine was started on September 21, 1943, and the culture showed a light growth at the end of the first week and was sterile after the second week, and subsequent cultures have been repeatedly sterile. The last one was obtained on June 7, 1944. A hysterotomy and tubal sterilization was done on November 18, 1943, at the fifth month of pregnancy.

Comment

These cases serve to emphasize at least three valuable assets of the drug. Most important of all, the drug has proved effective in eradicating infections which had proved resistant to other forms of chemotherapy including sulfathiazole and sulfadiazine (Cases 1 to 5 inclu-

sive). In Cases 7 and 8, chronic infections which had existed for years and given rise to serious obstetric complications were eradicated. No specific data are obtainable from the records of these two patients as to previous chemotherapy, but the history of both of them indicates a type of infection, which in our experience, has usually not responded well to other methods.

The drug was tolerated well by Cases 3 and 5 who had suffered severe gastrointestinal symptoms from other sulfonamides, and by Case 6 in whom sulfathiazole had produced a rapidly progressive anemia. The renal function in Cases 3 and 8, as well as in several others of the study, especially the one with bilateral renal calculi, was greatly impaired. Nevertheless, the drug was well tolerated by these patients, and only beneficial effects resulted from its administration.

From these observations we may conclude that eradication of the majority of infections due to *E. coli* may be expected from administration of the drug, and that it may be administered without fear of unfavorable reactions even in the presence of severe anemia or marked impairment of renal function.

Many of the obstetric patients with acute infections might have responded equally well to other sulfonamide drugs. However, the role of intestinal stasis in the production of pyelitis of pregnancy has been repeatedly stressed by those interested in the subject. This fact together with the low toxicity of the drug seemed to us to indicate its probable superiority for this type of infection.

In addition to patients with pure cultures of *E. coli* in the urine, seven patients showing cultures of other organisms have been treated. In five of these *E. coli* was also present. The other organism was *Aerobacter aerogenes* in two, *alpha Streptococcus fecalis* in one, and *Staphylococcus albus* in one, and both *Shigella dispar* and *Shigella paradysenteriae* in the other. The patient with *E. coli* and *Staphylococcus albus*, previously unsuccessfully treated with sulfathiazole, was cured and has remained well for fifteen months, suggesting that the *Staphylococcus albus* was probably a contaminant. The treatment was a complete failure in the patient with cultures of *E. coli* and *Shigella*. In the other three, there was symptomatic improvement, and the *E. coli* was eliminated, but the other organisms persisted. A sixth patient with *A. aerogenes* in pure culture was improved symptomatically, but the organism persisted in the urine. In the seventh, the cultures showed *Staphylococcus albus* and *alpha Streptococcus fecalis*, and no beneficial effect resulted from the treatment.

Discussion

We can only speculate as to the mode of action of the drug in accomplishing the results set forth. Alyea,⁷ Cook,⁸ and others have shown that large doses and high urine concentrations of the sulfonamide drugs

are not necessary in the treatment of urinary infections, and the average daily dose of sulfathiazole or sulfadiazine suggested by these authors is 1.5 to 2 grams. It might be argued from this that even the small

TABLE III. CONCENTRATION IN MG. PER 100 C.C. OF SULFATHIAZOLE IN THE BLOOD AND URINE OF PATIENTS RECEIVING SUCCINYL-SULFATHIAZOLE

Blood	0	0	0	trace	0	0	0	trace	1
Urine	12	1.75	—	—	—	4.7	7.6	—	—

amount of free sulfathiazole present in the blood and urine as a result of administration of sulfasuxidine may be the active agent in rendering the urine sterile. This argument seems untenable, however, in view of the very small amounts of sulfathiazole found in the blood and urine of those patients upon whom such determinations were made (Table III), and in view of the fact that several patients were successfully treated with this drug, whose infections had failed to respond to relatively large doses of sulfathiazole.

The only other alternative would seem to be that the tissues of the urinary tract are given an opportunity to rid themselves of the existing infection because the constant source of infection in the bowel is temporarily eliminated.

The reason for persistence of cure, in at least some of those patients who had previously exhibited chronicity or rapid recurrence of infection in spite of other forms of sulfonamide therapy, seems even more difficult to explain. Three possible explanations may be suggested:

First, elimination of the source of infection from the bowel for a period of three weeks may give the tissues of the urinary tract time to recover sufficient natural resistance to infection to protect them against recurrence.

Second, the beneficial effect exerted by the drug upon the intestinal tract may decrease the avenues for escape of organisms into the blood stream or lymphatic channels through which they may have been reaching the urinary tract.

Third, there may be certain strains of *E. coli* with a selective affinity for the urinary tract which are completely and permanently eradicated as a result of administration of the drug.

It seems probable that either the first or second of these mechanisms, or perhaps both of them, may be the explanation for the persistence of cure. It is for this reason that it has been considered advisable to continue the drug for at least two and preferably three weeks. In the majority of those patients cured, the cultures became sterile in less than a week after administration of the drug was begun, so that such an extended course was not necessary to effect an immediate cure.

As regards the third possibility, Meisser and Bumpus⁹ long ago demonstrated a selective affinity for the urinary tract upon the part of certain strains of *Streptococci*. In 1917, Helmholz and Beeler¹⁰ reported a

chance finding which suggested that there may be a similar selective affinity among strains of colon bacilli. Injecting intravenously into rabbits, strains of *B. coli* isolated from the urine of children suffering from pyelocystitis, these authors produced renal lesions in only 8, or 12 per cent, of 66 animals, and the tendency of the organisms to produce lesions in other organs was just as great as in the kidney. In similar experiments using a strain of *B. coli communior* isolated from the urine of a rabbit with a severe spontaneous urinary infection, pyelonephritis was produced in 22, or 70 per cent, of 32 rabbits, and only three of these showed lesions outside the urinary tracts. No other similar contributions have been found in the literature, however, and from discussion of the problem with several expert bacteriologists, we have gained the impression that little is known of specificity of strains of the colon flora, and that any attempt to settle this question experimentally would be met with insurmountable difficulties.

The chief objection to the drug is the large dosage required and the consequent expense to patients of small means. At the present time there is being subjected to clinical trial another drug, phthalylsulfathiazole (sulfathalidine), which from experimental results it is hoped will accomplish the same purpose in daily doses of no more than 0.1 Gm. per kilogram of body weight. We are investigating this drug at the present time, but as yet have not had sufficient experience with it to permit of sound evaluation.

Conclusions

Succinylsulfathiazole has been found effective in the treatment of urinary infections due to *E. coli*.

When administered in daily doses of 0.25 Gm. per kilogram of body weight, the urine is usually rendered sterile in less than one week.

Continuation of the drug in daily doses of 0.125 Gm. per kilogram of body weight for two more weeks seems to protect the patient against recurrence of infection.

The drug has proved effective against infections which had proved resistant to other sulfonamides and to mandelic acid.

The drug is not effective against infections due to organisms other than *E. coli*.

Because of its scant absorption and low toxicity, it is well tolerated by patients with impaired renal function, or severe anemia who would tolerate other sulfonamides poorly.

Theories of the possible mode of action of the drug are discussed. The most probable mode of action seems to be that elimination of the source of infection from the bowel permits the tissues of the urinary tract to throw off infection by means of their own resistant powers.

The large quantity of succinylsulfathiazole used in this study was made available through the courtesy of Dr. W. A. Feirer of Sharp and Dohme.

References

1. Poth, E. J., and Knotts, F. L.: *Proc. Soc. Exper. Biol. & Med.* 48: 129, 1941.
2. Poth, E. J., Knotts, F. L., Lee, J. T., and Inui, F.: *Arch. Surg.* 44: 187, 1942.
3. Poth, E. J., and Knotts, F. L.: *Arch. Surg.* 44: 208, 1942.
4. Poth, E. J.: *J. A. M. A.* 120: 265, 1942.
5. Johnson, S. A. M.: *J. A. M. A.* 122: 668, 1943.
6. Clay, R. C., and Pickrell, K. L.: *J. A. M. A.* 123: 203, 1943.
7. Alyea, E. P.: *J. Urol.* 47: 219, 1942.
8. Cook, E. N.: *J. A. M. A.* 115: 2079, 1940.
9. Meisser, J. G., and Bumpus, H. C.: *Arch. Int. Med.* 27: 326, 1921.
10. Helmholz, H. F., and Beeler, C.: *J. A. M. A.* 69: 898, 1917.

Discussion

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—As we review the titles of the papers that have been presented before this body during the past few years, we are struck by the scarcity of topics in female urology. It was the teaching of Dr. Clark and of Dr. Keene, my preceptors at the University of Pennsylvania, that female urology constitutes an indispensable part of the gynecologic specialty. I subscribe to this teaching. Therefore, it is particularly pleasing to me to be granted the opportunity to discuss this work that has been done so ably by a gynecologist.

Having had no personal experience with the use of succinylsulfathiazole in the treatment of urinary tract infections, my discussion consists of certain observations that are based upon a review of the literature, including Dr. Everett's manuscript and a limited experience in the management of urinary tract infections by other measures. As Cook stated recently, in simple uncomplicated infections of the urinary tract almost any of the sulfonamide compounds are effective in more than 90 per cent of the cases. We can state further that most acute uncomplicated urinary tract infections clear up within a short time whether treated by means of alkalization, acidification, alternation of the two, the older so-called urinary antiseptics, simple water diuresis, or by sulfonamides.

The few who do not respond and those with the tendency to recur, such as the ten cases referred to in Dr. Everett's Table II, offer a real opportunity for clinical investigation. His originality in thought and his success in the treatment of the *E. Coli* infections deserve commendation. It is unfortunate that a greater number of the recurrent or intractable cases do not result from this organism. Our experience indicates that *E. Coli* infections occur far less frequently than do those from other types of invaders, which appear not to respond to succinylsulfathiazole.

In the experimental investigation of succinylsulfathiazole, this drug has been shown not to remain entirely within the intestinal canal. Welch, by administering 5 milligrams per kg. per day of each drug to monkeys by gavage, found the average concentration in the blood of succinylsulfathiazole to be 3 mg. per cent, and of sulfathiazole to be 0.8 mg. per cent. Apparently, the latter is formed by hydrolysis.

Poth detected an average of 2 mg. per cent of succinylsulfathiazole and 0.95 mg. per cent of sulfathiazole in the blood stream, following his routine dosage in the human being. While such concentrations are desirable in the treatment of urinary tract infections, by the same token, they may be distinctly harmful to the patient. Poth, Clay and Pickrell, and Johnson have reported a total of four unfavorable constitutional reactions to succinylsulfathiazole—one of which was fatal. These reactions were ascribed to either sensitivity or idiosyncrasy to sulfathiazole and emphasis was laid upon the danger of prolonged administration or intermittent application of sulfonamide therapy. Each of those writers recognized that the ingestion of succinylsulfathiazole is attended by the risk of an untoward response.

Patients who receive this drug—as is true of all sulfonamides—should be kept under careful observation, for it cannot be administered without fear of unfavorable reactions.

In considering the mode of action of succinylsulfathiazole, the essayist pictures the most likely effect to be that of alimentary bacterial depletion with subsequent or concomitant assertion of the natural resistant and recuperative powers of the urinary tract. The chronology of events gives reason to question this conclusion. Poth found that the intestinal flora is about depleted in 93 per cent of the cases at the end of a week. Of 41 cases treated by Everett, 91 per cent of the urines were rendered sterile—usually in less than a week. It is doubtful, that this round the corner therapy could produce simultaneous results in both the intestinal and the urinary tracts, if the latter result is dependent upon completion of the former. The time relationship suggests a dual action, and this suggestion is supported by investigative studies. Poth found the urinary excretion of sulfathiazole to average 0.34 mg. per cent, and that of succinylsulfathiazole to average 0.38 per cent following his routine dosage. Everett found the urinary concentration of sulfathiazole to vary from 1.75 mg. per cent to 12 mg. per cent. He did not report the urinary concentration of succinylsulfathiazole. The remarkable susceptibility of *B. coli* organisms in the intestinal canal to this type of therapy has been demonstrated repeatedly and these organisms should react similarly in the urinary tract. Many writers have emphasized the low dosage requirements in other forms of sulfonamide therapy for urinary infections. It seems reasonable, therefore, that Dr. Everett's results are due first, to local action of these drugs as they are excreted by the kidneys and second, to intestinal bacterial depletion.

DR. J. MASON HUNDLEY, JR., Baltimore, Md.—For many years considerable interest has been centered upon the subject of urinary antiseptics, initiated in some measure by the work of Shohl and Janney¹ in 1917, who showed that the growth of *Escherichia coli* was inhibited by changing the hydrogen-ion concentration of the urine. Some years later Clark² and Helmholtz introduced the ketogenic diet, its essential factor being the high fat content in relation to the carbohydrate component. Due to the incomplete metabolism of the fats, a condition of acidosis is produced with the outpouring of ketone bodies in the urine, chiefly beta-hydroxybutyric acid. It has been shown by Fuller³ that it is this ketone body in the presence of markedly acid urine that produces the desired bactericidal effect. This diet, as will be remembered, was difficult to carry out as it frequently produced severe gastrointestinal disturbances.

Another advance was the introduction of mandelic acid. This substance, which is secreted unchanged, is efficacious only in a markedly acid urine, the acidity being accomplished by the administration of ammonium chloride. Ammonium mandelate, as it is now produced, is of use in patients in whom sulfa therapy is not tolerated and continues to be used in selected cases.

No real success was attained, however, in the treatment of urinary tract infections until the introduction of sulfanilamide and its closely related substances. The most popular urinary antiseptics today, I believe, are sulfathiazole, sulfadiazine and sulfamerazine, and probably the latter evokes fewer untoward reactions than any of its associated compounds. As is well known, after continued use of the sulfanilamides, organisms originally susceptible may become fast and the drug be ineffective. The use of sulfasuxidine for persistent urinary tract infections, particularly those due to the *Escherichia coli*, seems to be a distinct advance and well worthy of trial. In this relation I have had no personal experience, having employed it only with intestinal operations and especially in the preoperative treatment of complete perineal lacerations.

Sulfasuxidine therapy will be of inestimable value in treating pyelitis with pregnancy when the usual infecting *Escherichia coli* is not susceptible to the sulfa group.

In using any type of chemotherapy for urinary infections, it is first obligatory to relieve any obstructive lesion. If such a condition is not removed, there is no permanency of urinary sterilization, for with cessation of therapy there is soon a return of the infection.

I agree with the essayist that permanent cures are difficult to explain when they are initiated by only a temporary sterilization of the bowel content, this being complete or more frequently incomplete.

When one reviews some of the opinions in regard to the lymphatic relationship between the bladder and kidney and especially between the large bowel and kidney, it is more difficult to understand how a permanent cure could be produced. Franke⁴ has demonstrated that lymphatics from the large intestine pass over the capsule of the kidney, that the kidney has a rich network of lymphatics that emerge at the hilum, and that there is a connection between these lymphatics and those of the capsule. Mayer⁵ is of the opinion that the lymphatic connection only occurs between the colon and the right kidney and that pathologic changes of the intestinal wall are necessary before a transmigration of organisms can take place, probably explaining, if he is correct, the intermittency of kidney infections. Regardless of these anatomic findings, which may not be constant, sulfasuxidine would appear to be of great value in eradicating persistent urinary infections due to the *Escherichia coli*.*

DR. EVERETT (closing).—Dr. Payne spoke of the possible dual action of this drug, and he is quite right in emphasizing this point. I emphasized the mode of action through the intestinal tract particularly because some of these cases had not completely cleared up with the administration of sulfathiazole alone. It is possible that the two modes of action together may be the final answer, but I do believe that the elimination or reduction of the intestinal flora is at least partly responsible for the results obtained.

Dr. Hundley stressed the eradication of urinary obstructions, and I have mentioned that point in the paper also. Our clinic under the leadership of Dr. Hunner has for years stressed the importance of establishing adequate renal drainage in the treatment of infections as well as many other diseases of the urinary tracts. Every possible effort was made to eliminate any discoverable obstructive lesion in each of these cases.

*1. Shohl, A. T., and Janney, J. H.: J. Urol. 1: 211-228, 1917. 2. Clark, A. L.: Proc. Staff Meet. Mayo Clinic 6: 605-608, 1931. 3. Fuller, A. T.: Lancet, 1: 855-856, 1933. 4. Franke: Ergebn. d. Chir. u. Orthop. 7: 671, 1913. 5. Mayer: München. med. Wchnschr. p. 1479, 1913.

MATERNITY CARE IN THE UNITED STATES—PLANNING FOR THE FUTURE*

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MY REMARKS this evening will be devoted to the consideration of the development of a nationwide maternity service.

The object of this Society, as stated in its constitution 68 years ago, was the promotion of knowledge in *all* that relates to obstetrics, the diseases of women, and abdominal surgery. The distinguished fellows of the Society and its guests have presented and discussed in the annual meetings many of the great clinical advances made in obstetrics and gynecology during this long period. Rarely, however, do the transactions of the Society reveal any discussion of the ways and means whereby the great knowledge and skills developed in these specialties could best be made available to the greatest possible number of women in the United States.

Dr. Taussig in his presidential address of 1937, "The Story of Prenatal Care," spoke as follows of Dr. Ballantyne: "The dawn of the twentieth century found his spirit rising with the hope of an age when all expectant mothers would be properly cared for."

In the presidential address of Dr. Holden in 1939, and of Dr. Litzenberg in 1941, significant statements were made. Dr. Holden said, "We can no longer retire to our clinics and laboratories but must take our proper place in all broad programs of social welfare which affect the health of our people" and Dr. Litzenberg stated, "Medicine certainly cannot attain its proper place in society by resisting all of the impacts of social change."

Advances in the science of obstetrics have been truly great during the history of this society. Have methods of making available and applying this knowledge of maternity care on a nationwide basis been given sufficient consideration?

I was first requested to speak on obstetric care in wartime, but later broadened the title since wartime measures must be considered in relation to what has gone before and what may occur in the future.

Twenty-five years ago, there were but practically few specialists in obstetrics. Most women were delivered by the family doctor or kindly neighbor women. Today, a growing number of women in the United States recognize the better care provided by physicians specially trained in obstetrics, and the demand for maternity care by specialists is rapidly increasing.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

Graduate education and experience definitely planned to train specialists in obstetrics, or obstetrics and gynecology, have developed within the lifetime of many of you here. Before the second World War not more than 2,500 physicians limited their practice to this specialty, and less than three-fourths of these were Diplomates of the American Board of Obstetrics and Gynecology. More than two million, or 4 out of 5, maternity patients in 1912 did not receive the expert care which a specialist in this field can give. One basic guide for future planning should be the following principle:

That in the United States *all* maternity patients should have advice and treatment throughout the maternity cycle by or under the immediate supervision of a doctor of medicine recognized as a specialist in obstetrics.

Eight years ago only two-fifths of all births in the United States occurred in hospitals. More than two-thirds of the births now occur in hospitals. Although 84 per cent of maternity patients in urban areas obtained hospital care in 1942, only 45 per cent of those in rural areas were cared for in hospitals. What plans should be made for providing hospital maternity care for the million women now unable to secure such care each year? In planning for the future, a second basic guide should be the following principle:

That *all* maternity patients should have care during labor and during at least the first 10 days after delivery in hospitals equipped and staffed to provide all possible safeguards to the health of mother and infant, and all maternity patients with serious complications during pregnancy should have care in such hospitals.

How can the objectives stated in these two principles be attained? There would appear to be three major steps:

1. Training the additional obstetricians needed.
2. Building the additional hospital facilities needed.
3. Developing a plan which will assure the effective utilization of such specialists and facilities in providing care for all maternity patients without regard to their economic status.

Training Additional Obstetricians Needed

Theoretically, all obstetric care and teaching in the United States could be provided by approximately 10,000 specialists in obstetrics, including the resident obstetricians in training, if the obstetricians and hospital facilities needed were geographically so located as to be accessible for 2,500,000 maternity patients each year. This estimate is calculated on the premise that all births would be occurring in hospitals, with one obstetrician or resident obstetrician in training for approximately every 250 maternity cases each year. (Since students

and interns, under supervision, would deliver many women in the teaching hospitals, the number of patients actually attended by the senior teaching staff would be considerably less than the figure of 250 used in this calculation.)

In 1942, approximately 2,500 physicians limited their practice to obstetrics or obstetrics and gynecology. The American Board of Obstetrics and Gynecology had examined and certified as specialists less than three-fourths of these physicians. At least 7,500 additional fully qualified obstetricians are needed in the United States and a plan should be made for their training. This number could be trained in 10 to 15 years after the war.

Table I shows the number of additional obstetricians needed in each State.* The 439 hospitals in which 1,200 or more births occur each year have a total of approximately 720,000 births each year. If all hospitals reporting 1,200 or more births a year could meet necessary standards of approval for the 3-year training of residents in obstetrics

TABLE I. NUMBER OF ADDITIONAL OBSTETRICIANS NEEDED IN EACH STATE TO PROVIDE ONE OBSTETRICIAN FOR EVERY 250 LIVE BIRTHS

Alabama	262	Nebraska	76
Arizona	28	Nevada	11
Arkansas	164	New Hampshire	37
California	390	New Jersey	254
Colorado	71	New Mexico	54
Connecticut	10	New York	422
Delaware	15	North Carolina	324
District of Columbia	4	North Dakota	43
Florida	128	Ohio	446
Georgia	259	Oklahoma	155
Idaho	45	Oregon	72
Illinois	432	Pennsylvania	586
Indiana	267	Rhode Island	42
Iowa	168	South Carolina	182
Kansas	118	South Dakota	48
Kentucky	246	Tennessee	230
Louisiana	199	Texas	501
Maine	62	Utah	55
Maryland	105	Vermont	27
Massachusetts	210	Virginia	237
Michigan	407	Washington	117
Minnesota	180	West Virginia	162
Mississippi	220	Wisconsin	229
Missouri	191	Wyoming	21
Montana	41		

or obstetrics and gynecology, and if for approximately every 1,200 births occurring annually, they would graduate each year one resident completing 3 years' training, there would soon be an annual increase of approximately 600 in the number of obstetric specialists. When such a training program was fully operating, each teaching hospital would have a first-year, a second-year, and a third-year resident in training for each 1,200 births, or a total of approximately 1,800 residents in training.

*In addition to number of physicians limiting their practice to this specialty at time of Procurement and Assignment survey in 1942.

There should be no difficulty in obtaining this number of residents immediately after the war when thousands of young physicians with little or no previous opportunity for graduate training will be released from military service. The continuing supply of approximately 600 residents in training to be appointed each year would be approximately 10 per cent of the number of physicians completing internships each year before the war. The 600 physicians completing their 3-year resident training each year would provide the additional specialists needed until some 10,000 qualified obstetricians were available. After this quota was reached, about 300 new specialists would need to be trained each year for replacements due to death or retirement.

If obstetrics and gynecology were combined in the service of the specialists under discussion, and it is believed that they should be, some modification would be necessary in the estimated number of specialists and hospital beds required.

Building Additional Hospital Facilities Needed

Approximately 30,000 additional beds are needed to provide hospital care for all the maternity patients now delivered at home. Table II shows the number of additional beds needed for each State. Some of the beds should be in maternity units of general hospitals which should be constructed for the most part in small communities, and others would probably be in 20- to 40-bed maternity hospitals to be constructed in rural areas where the establishment of a general hospital would not be practicable. Under Government postwar building programs to absorb manpower released by the Armed Forces and war

TABLE II. NUMBER OF ADDITIONAL HOSPITAL MATERNITY BEDS NEEDED IN EACH STATE TO PROVIDE HOSPITAL CARE FOR ALL DELIVERIES NOW OCCURRING AT HOME

Alabama	1,849	Nebraska	259
Arizona	125	Nevada	9
Arkansas	1,143	New Hampshire	46
California	453	New Jersey	296
Colorado	239	New Mexico	313
Connecticut	56	New York	710
Delaware	48	North Carolina	2,060
District of Columbia	55	North Dakota	126
Florida	673	Ohio	1,316
Georgia	1,599	Oklahoma	763
Idaho	81	Oregon	55
Illinois	875	Pennsylvania	1,903
Indiana	843	Rhode Island	67
Iowa	502	South Carolina	1,268
Kansas	375	South Dakota	141
Kentucky	1,785	Tennessee	1,497
Louisiana	1,025	Texas	2,380
Maine	212	Utah	102
Maryland	530	Vermont	78
Massachusetts	256	Virginia	1,389
Michigan	956	Washington	79
Minnesota	454	West Virginia	1,103
Mississippi	1,648	Wisconsin	527
Missouri	1,059	Wyoming	38
Montana	47		

industry, the construction or expansion of hospitals to provide this number of additional maternity beds would be possible over a period of 10 years and would cost on an average approximately \$15,000,000 during each year of construction, probably with larger expenditures in the earlier years of the period. This cost is estimated on the basis of \$5,000 per bed. The location of additional hospitals should be determined on the basis of need in relation to the number of maternity beds in existing hospitals, the number of births in given areas, and the transportation problems involved. Ambulance service (automobile and possibly airplane) should be affiliated with the hospitals in some areas.

Every hospital should have proper facilities for obstetricians on the staff to provide prenatal care for all the patients living near enough to come to the hospital for this purpose. The time and energy of physicians would be conserved if they had their offices in the hospital where all their patients received hospital care. Patients would be more likely to receive all the laboratory, x-ray, and other special diagnostic services needed if these were available in the same building in which they received office care. In some of the less populated areas, maternity patients should be able to receive prenatal care in health centers near their homes, the obstetricians on the staff of a near-by hospital treating patients in such health centers perhaps one day each week. The smallest maternity unit of a general hospital or small maternity hospital should have at least 20 beds, which would provide accommodations for between 500 and 600 maternity cases per year. Twenty maternity beds would serve a population of approximately 25,000, and two obstetricians could provide all maternity care for most areas with this population. Maternity units serving sparsely populated areas might need to have accommodations near by where women living long distances from the hospitals could be housed for a week or more before the expected date of confinement.

In order to provide hospital maternity facilities wherever needed, Federal grants should be made available for their construction. These grants should be made only when the new hospital or enlargement of existing facilities are in accordance with a State-wide plan of the official State health agency for hospital facilities—which had been made after a thorough survey of the needs of the State and which would assure the most effective utilization of such facilities. The architect's plan and the standards of construction should, of course, meet recognized modern standards for satisfactory maternity units.

Some of the Present Conditions Affecting Future Planning

Eight years ago in the programs initiated under the Social Security Act, provisions were made for the extension and improvement of health services for mothers and children throughout the United States. Since that time, the State and local health agencies have greatly increased health education in this field, established clinics for prenatal and in-

fant care, employed thousands of public health nurses, who as a part of their duties, advise and assist women in the prenatal and postpartum periods, established and enforced higher standards of hospital maternity services, provided postgraduate training in obstetrics for thousands of physicians, public health nurses, and hospital nurses, and initiated and carried out many studies of maternal morbidity and mortality. Approximately \$10,000,000 is now expended each year under this nationwide maternal and child health program; and these services have undoubtedly been in part responsible for the decrease of more than 50 per cent in maternal mortality rates during these 8 years.

Insurance for loss of wages during unemployment and to provide income during old age has been firmly established under the Social Security Act and now covers more than 40,000,000 people, or one-third of the entire population of the United States.

Voluntary insurance for hospital care began approximately 10 years ago, and now provides protection for between 15 and 20 million people in the United States. Approximately one-fourth of all hospital care provided under Blue Cross insurance plans is for maternity care. Medical-service plans and group health insurance cover the cost of medical care on a prepayment basis for more than 3,000,000 people today. Under the Michigan Medical Service plan, for example, obstetric and gynecologic services represent 36 per cent of the total cost of all service provided. The protection afforded by unemployment, old age, and health insurance is thoroughly appreciated by most American families.

It appears likely that next decade will see a rapid expansion in prepayment or taxation plans for financing the costs of medical and hospital care. Whether such plans will ultimately be financed on a voluntary basis similar to Blue Cross, or by compulsory pay roll deduction, general taxation, or combinations of these, is uncertain. Present trends indicate that the method of paying for medical care is rapidly changing from the variable individual expenditure to new bases which more equitably distribute the cost.

The extent to which Government is now directly concerned with provisions for maternity care is significant. About 15 per cent of all births now occur in Government hospitals and the cost of most of this care is paid from tax funds. State and local public agencies arrange and pay for the care of many other maternity patients in nongovernmental hospitals. The emergency maternity and infant care program, established as a wartime service, is providing care this year for approximately 15 per cent of all maternity cases. It may be conservatively estimated that between one-fourth and one-third of all maternity cases in the United States are now having their care paid for from public funds,

A few words concerning the EMIC program. Fifteen months after war was declared, when it became obvious that thousands of the wives of the enlisted men needed help in planning and financing their maternity care, the Congress made funds available to the State health agencies, through the Children's Bureau, to provide medical, nursing, and hospital maternity and infant care as a matter of right for the wives and infants of enlisted men in the four lowest pay grades of the Armed Forces.

This program as developed and administered is on the whole quite satisfactory to the patients and their families, to hospitals, and to the general practitioners who at present provide most of the maternity care in the United States. Many specialists in obstetrics, however, feel that the rates of payment for maternity care under the program should have been more in line with their usual charges for private patients rather than based upon the usual charge of general practitioners. When the program started, the Children's Bureau suggested a differential rate of payment between specialists and general practitioners, but the physicians on the Advisory Committee of the Children's Bureau recommended no differential in the rates. This month 20 obstetricians, most of them in private practice, met with the Children's Bureau and again expressed the opinion that it would be very difficult to work out a practicable method of establishing different rates of payment to the general practitioner and to the specialist.*

In many communities the specialists in obstetrics have not fully realized the valuable service they could render under this program by assisting the State agencies in arranging as far as possible for the general practitioners to call them for consultation and help with complicated cases. The preparation of lists of the best-qualified consultants in various areas of each State has been most difficult, and in only a few States have the obstetricians actually assisted the State health departments in selecting the best-qualified men for such lists. The question of requiring obstetric consultation, where available, when serious complications occur, should be receiving more consideration. If the specialists in obstetrics were being called by general practitioners when serious complications occur, not only would there be better care of the individual patient, but there would also be an improvement in the quality of maternity care by general practitioners as a result of the educational value of consultation.

The administrative framework and policies for the EMIC program were, of necessity, drafted and applied to fit a temporary nationwide program which had to be put into operation in as short a time as possible. Since many of the individuals eligible for care were moving

*Since this article was submitted for publication the Children's Bureau of the Department of Labor has amended its policies for the administration of the EMIC program to provide, at the option of each State agency, differential rates of payment to specialists for care confined to their specialty if the rates do not exceed by more than 50 percent the maximum rates adopted by the State agency for general practitioners and do not exceed the rates customarily paid to such specialists.

from State to State, and many physicians and hospitals near State lines provided care for patients from 2 or more States, policies of administration had to be reasonably uniform between States. No comparable program had been undertaken before in this country. Many State health departments had little or no experience in the administration of public medical-care programs. It is really quite remarkable that, at the end of the first year, care was being authorized under the program for more than 40,000 new patients each month and in all States and Territories and it appears now that care, for between 15 and 20 per cent of all maternity cases in the United States will be provided under this program during the next year. The Children's Bureau believes, however, that many of the methods of administration that have, of necessity, been adopted for this emergency wartime program, designed to meet the needs of a selected group of maternity patients, would be unsatisfactory for a more permanent nationwide maternity service.

Many individuals have asked to what extent Government will be concerned with provisions for maternity care after the close of the war when authorization for the EMIC program will have expired. No one can predict what the sentiment of the people will be—and it is they who will determine what responsibility Government will have in this field. Fortunately, the EMIC program has provoked and will continue to provoke much discussion concerning the best method of providing and financing maternity care.

Planning of national health programs to meet the needs of citizens over the world is widespread at the present time. In the United States labor, farm, and other citizens' groups, Federal, State, and local governmental agencies, and several State or local medical societies are proposing or experimenting with a variety of tax-supported or insurance plans. Organized medicine has made it clear what it does *not* want, but has left everyone uncertain as to what it does want. A realistic attitude on the part of the practicing physicians toward changes which are taking place and intelligent leadership in the medical profession for planning for the future are needed urgently.

The problem of how to pay for medical or hospital maternity care now confronts more than 21½ million families throughout the United States each year. For many of these families the cost of maternity care is a major economic problem. Studies show that in 1942, when war industry was rapidly expanding, 62 per cent of the families of two or more individuals in the United States had money incomes of less than \$2,500 a year. Less than 10 per cent of such families had money incomes of \$5,000 or more a year. In the peacetime years of 1935 to 1936, 85 per cent of such families had incomes of less than \$2,500 and only 3 per cent of the families had incomes of \$5,000 or more. Few of these families under present methods of financing can pay the cost of high quality medical and hospital care. Yet all these

families should receive needed care by physicians specially trained in obstetrics, and this care should be given in modern maternity hospital facilities. Methods of providing the best possible maternity care to all families living in the more than 3,000 counties of the United States must be studied.

If the additional specialists and hospital facilities needed, as outlined in the early part of this paper, are made available, what type of plan would be most likely to assure their effective utilization in providing good maternity care in all parts of the United States? Good maternity care for all families of the United States cannot be assured if we depend upon the ability of a few to pay the costs on the sliding scale of fee for service and the present haphazard efforts to provide care for those unable to pay.

The cost of providing all the maternity care needed in the United States should be determined and sound plans for financing and provision of such services should be agreed upon.

A careful estimate indicates that the total annual cost of providing medical and hospital care for all maternity cases could be in the neighborhood of \$250,000,000. Included in this amount is an estimate of the total net income of 10,000 obstetricians at a beginning rate of \$2,000 net per year for first-year residents and a maximum of \$20,000 net per year for chief obstetricians in the largest teaching centers. Also included is the total cost of hospital care for all maternity patients, as well as maintenance of physicians' offices in the hospitals and all laboratory or other diagnostic and consultation services. The \$250,000,000 is equivalent to 60 cents per month for each family in the United States.

Obstetricians will not be accessible to all maternity patients until these physicians are assured adequate income irrespective of the ability of the community to provide it. Residents might be appointed under an agreement to practice in a hospital in a smaller community for at least 5 years after completing their training. Remuneration of physicians must be commensurate with the training and experience of the individuals, the responsibilities of their positions, and the quality of services provided.

If a nationwide plan for maternity care, financed entirely from the revenues of general taxation or from insurance contributions supplemented by tax funds, were to be adopted, some of the principles of administration which should be observed may be outlined briefly as follows:

Administration should be primarily a local community responsibility and the hospitals of the future should become the community centers for all preventive and curative services. Physicians participating in the service in any community could determine whether they wished to be paid on a case basis or a salary basis. I believe that the appointment by hospitals of full-time obstetricians to provide care for all

maternity patients seeking care at the hospital or its affiliated health centers will ultimately be found to be most satisfactory for all concerned. Patients should have free choice among the obstetricians and hospitals accessible to them.

Minimum qualifications required for the appointment of obstetricians to hospital staffs would have to be established, and within 10 or 12 years, it could be required that all obstetricians on hospital staffs have the training and experience required of Diplomates of the American Board of Obstetrics and Gynecology. Until a sufficient number of obstetricians were trained, there would be many communities in which maternity care could be provided only by the general practitioners now including obstetrics in their practice. The responsibility for the maintenance of a high quality of medical and hospital service for all hospitals in a region, for consultation, and for periodic review of cases in the medium-sized or smaller hospitals should be placed on the staffs of the medical school and other teaching hospitals with which all other hospitals in the region with maternity services should be directly affiliated. All specialists should have opportunity each year to keep fully informed on advances in this field of medicine and to have readily available all the diagnostic and treatment facilities that may be needed for the best possible care of maternity patients.

To assure maintenance of the hospital maternity services in any community, regardless of its economic status, the hospitals must be freed from their dependence upon contributions or upon the overcharging of private patients to make up for the loss through free services. Any approved hospital should be paid from public funds on a cost basis for providing all in-patient maternity care and care for newborn infants and the cost of maintenance of facilities for prenatal care and all laboratory, x-ray, and other special diagnostic services for maternity patients. Payments from public funds for hospital care should be dependent upon (1) the hospital's maintenance of established standards of equipment and services, (2) upon agreements to provide within the limits of their accommodations, maternity care for any woman applying for such care, irrespective of her residence, race, or economic status, and (3) upon the affiliation within a region of all maternity services from the first-line university and teaching hospital centers through medium-sized hospital maternity services to the smallest hospital or maternity-home, in order that consultation, diagnosis, and other services of the larger hospitals might be made as readily available as possible to the smaller hospitals.

Medical and hospital maternity care should be supplemented by education of the public—through the work of the public health nurses and through the press, radio, and other media—regarding the need for and value of good maternity and infant care. The public should be given instruction, too, as to the proper diet and hygiene for the mother during the maternity cycle, and for her baby, and how such a diet can be

obtained within the resources of the ordinary family. Also, household-aid services should be established in all communities to provide help when needed in the home during the hospital confinement and convalescence of the mother.

If a nationwide plan for comprehensive health services for the whole population were adopted, the program for maternity service here outlined would become a part of a national health program.

I am confident that the ways and means will be found for assuring all expectant mothers the best possible maternity care. This objective cannot be attained without proposing plans, studying them carefully, and modifying them as necessary, until they are acceptable to the citizens receiving care as well as to the professions providing care.

The suggestions in this paper are those of the author. The Children's Bureau before committing itself to any definite policy will continue to study and review with its advisory groups the many problems relating to extending and improving health services for mothers and children in the United States.

Discussion

DR. JOHN R. FRASER, MONTREAL, CANADA.—It has been a great privilege to hear one who is so conversant with obstetric conditions outline what he feels should be the future plan to control the management of pregnant women in the United States.

There are two fundamental principles which govern this scheme: first, that all pregnant women in the future shall be under the control and management of an obstetric specialist; and, second, that all obstetric patients shall be hospitalized. Of course, that is an all-embracing and most important statement, but to put it into effect is another matter. I thought Dr. Daily's suggestion excellent, that one of the first things should be a three-year training of men who are considering life as an obstetric specialist. That is naturally important as the general surgeon has already determined so well. The statement that 84 per cent of pregnant women today in urban localities are hospitalized and only 45 per cent in the rural communities is of interest to me. In Canada, 47 per cent only of our pregnant women are hospitalized and this is one of the basic obstacles to the whole scheme. In the sparsely settled areas, it will be very difficult, at least for a long time, to bring about any hospitalization scheme, desirable as it may be.

I would like to discuss this problem from the angle of our Canadian situation because we are in the midst of formulating what I think is a very important scheme. In certain parts of Canada, for instance in Alberta, they have taken a step which is extreme in one direction, for they have set aside \$700,000 so that pregnant women shall receive treatment free. Across the country we come to the opposite extreme where Quebec gives us 34 cents a day for the mother and the same amount for the baby. That is all the State offers to one who cannot afford hospitalization. To correct this great divergence in planning, the Canadian Government has before Parliament a Health Insurance Act which has been formulated, I am glad to say, in association with organized medicine. The profession has participated from the very beginning and, while we have not been able to direct it by any means, we have been able to follow along with it and give advice.

Every person in the country, 16 years of age and over, will be taxed \$9.50 per annum which will provide for medical care of all descriptions, including a complete obstetric service. We believe that will provide a fund of something like a

hundred and seventy odd millions, and it is hoped that the obstetric patient will share generously in that fund.

From all these insurance schemes, there has arisen a special problem for the teaching hospital, namely, that the more we assist and provide for the obstetric patient the less material we are to have for instructing our students. We are already having much more difficulty getting teaching material and it has been definitely written in this new Bill that any patient receiving public funds shall be considered to be a patient upon whom teaching may take place. This is a fundamental question because we have found already with any of these insurance schemes that it has encouraged a feeling on the part of the patient against being used for teaching purposes. As the Labor Party announced in Parliament, "We do not propose to be guinea pigs any longer."

In conclusion I would like to remind you that the United States government by a policy of education and by the efforts of agencies in Washington and allied associations has been able throughout the country in the last 15 or 20 years definitely to lower the mortality rate. The same process has been seen in Canada. Before adopting any scheme that may be formulated, we must bear in mind that we should maintain what we have at present and not upset that important doctor-patient relationship which is fundamental in medicine. We should also remember that the system we have at the present time has not done too badly.

DR. FRED L. ADAIR, CHESTERTON, IND.—In approaching a discussion of this subject, we ought to begin with a consideration of some very important fundamental principles which are involved in our ideals of democracy. There are certain things that we have to accept in a democratic form of government and among these are equal opportunities for every citizen insofar as it is possible to supply these. Two basic requirements in securing these equal opportunities are education and health. These two basic ideas are very closely tied one with the other. My remarks will be mostly confined to the basic principles of health.

We have to look at a maternity and infancy program not as a program in itself, but as one which is definitely tied in with all health activities. In developing a maternity and infancy program it should be integrated with other health as well as educational activities.

Now one of the principles of democratic government which I believe is fundamental for all governmental activities is local self-government. Federal taxation, or even State taxation, has certain important objectives. One of these is to pay the necessary expenditures of governmental activities. The other is to provide funds for the equalization of essential activities in various communities. Any federal funds which are appropriated should be viewed from these two angles, one to pay the necessary expenditures of the federal government; the other to distribute these funds so that under local self-government these funds can be, as nearly as possible, equalized for the attainment of these objectives which I have mentioned.

If large proportions of these funds appropriated by federal and state governments could be used for hospitals and equipment for the practice of modern medicine, we could gradually evolve a system which would preserve the individuality of the medical profession, and, at the same time, provide through these facilities, improved opportunities for practice by the medical profession. This would result in the type of service which we would like to have every mother in the country receive. I do not know how the organization of such a plan can be worked out except by evolution, and by the trial and error method. It is quite possible that the same method may not apply to different areas.

With reference to hospitals, it seems to me that there should be first a relatively simple setup which would be adequate for the care of the more ordinary medical problems, including maternity cases. There should be in addition institutions for providing more specialist care in larger areas so that it could be possible to shift

patients from communities where relatively simple care was enjoyed, into areas where much more highly specialized care could be supplied.

In brief, this represents my viewpoint. We must work out a health program with reference to maternal and infancy care which is in accordance with our democratic ideals.

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD.—Quite obviously Dr. Daily's paper raises a number of issues, controversial issues it is true, but living issues and issues of the utmost importance to all of us. Three questions which it raises seem to be deserving of our particular consideration, as follows: (1) What will be the

DISTRIBUTION OF FAMILY INCOME IN THE UNITED STATES BY INCOME LEVEL 1935-36

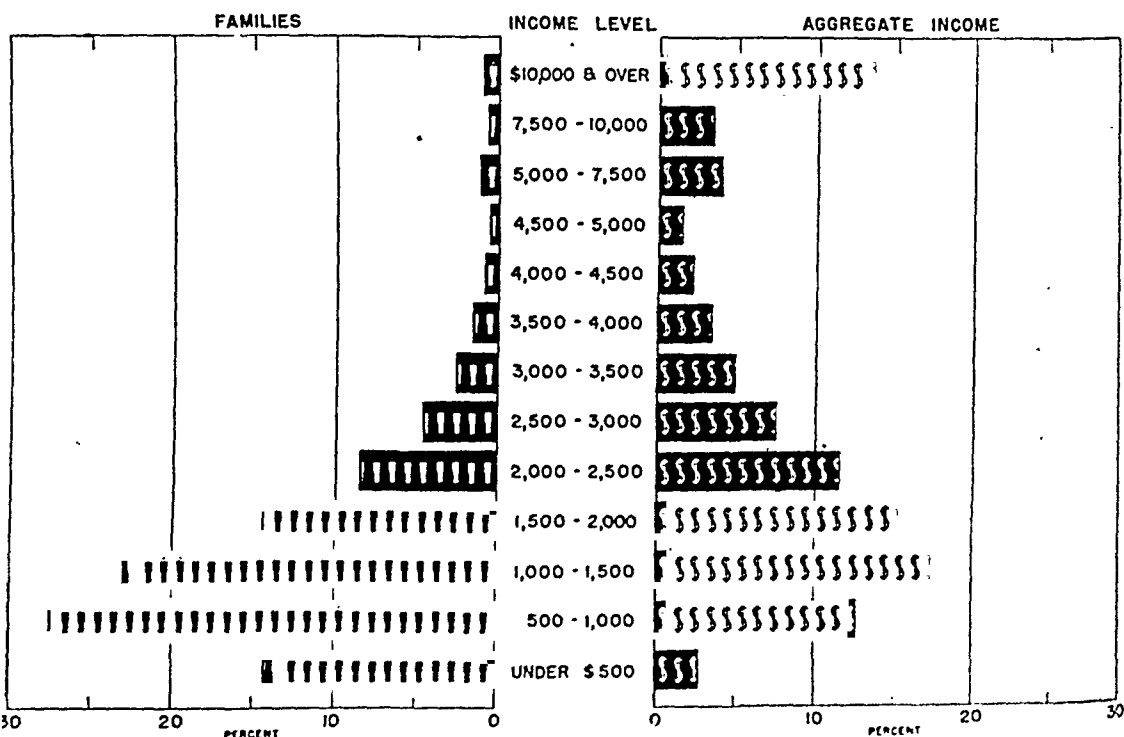


Fig. 1.—This chart may be read either by length of bars or by symbols. Each figure symbol represents 1 per cent of all families or 294,000 families. Each dollar symbol represents 1 per cent of aggregate income of all families or \$476,792,380.

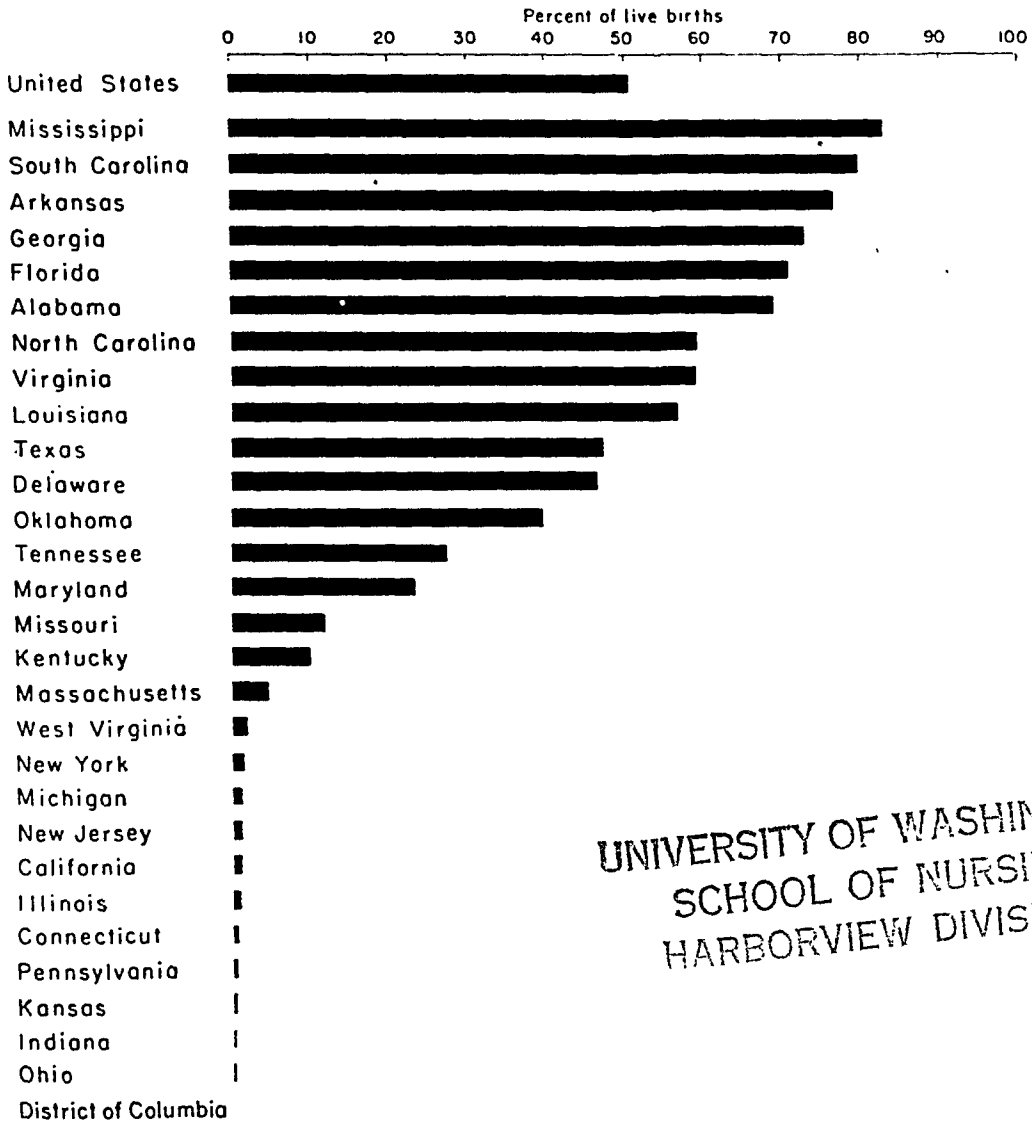
effect of this program which he visualizes on the quality of maternity and infant care in the United States? (2) What will be the effect of this program on the private practice of obstetrics? (3) And what will be its effect on the individual initiative and enterprise of obstetric specialists?

Fig. 1 shows, as of 1935 to 1936, the percentage of families which fall into the various income groups: 1 per cent having \$10,000 or over, and so on down. It can be concluded from these statistics that some 41 per cent of our families in 1935 to 1936 received incomes of \$1,000 or under. I think that everyone here will agree that such a level of income is not adequate to pay for the best obstetric care with its increasing complexities.

Yet, that is not all. Those who are acquainted with such matters tell us that people in these lower income brackets have illnesses and require the attention of doctors with twice the frequency of those in the upper income brackets, and we all know that the birth rate is much higher in these lower income groups. Ac-

cordingly, while we may say that some 40 per cent of the families in 1935 to 1936 had income levels under \$1,000, this group required much more than 40 per cent of the total obstetric and medical care needed by the nation. What has happened to these people in the past? They have been taken care of, for the most part, by county, state and federal funds, but it is well to recall that a large number of them have not been taken care of at all.

PERCENTAGE OF NEGRO LIVE BIRTHS WITH NO MEDICAL ATTENDANT
UNITED STATES AND EACH OF THE 29 STATES WITH 500 OR MORE NEGRO LIVE BIRTHS, 1940



UNIVERSITY OF WASHINGTON
SCHOOL OF NURSING
HARBORVIEW DIVISION

U.S. Department of Labor
CHILDREN'S BUREAU.
Chart No B40-9

Based on data from U. S. Bureau of the Census

Fig. 2.

Fig. 2 shows that in many of the southern states over 80 per cent of the Negro births occur without benefit of medical attention. It is instructive to note that in these very same states in which so many Negro births are without benefit of medical care, that the maternal mortality is the highest. This of course may be a coincidence, but there is valid evidence indicating that a relationship exists between

the fact that so many people in these lower income brackets receive no medical care at delivery, and the higher maternal mortality rate.

It is my feeling that the plan recommended by Dr. Daily would go far toward improving obstetric care in these areas and among those groups who do not have adequate income to provide for private obstetric care; and, by the same token, it should improve maternal and infant mortality rates the country over.

What effect would this plan have on private practice? I would direct your attention to the right side of Fig. 1. While it is true that families with incomes of \$10,000 and over represent only 1 per cent of the families of the United States, they received 13 per cent of the aggregate income. It can be deduced further from these statistics that the families, who have an income of \$2,500 and over, receive some 30 per cent of the aggregate income. Now these families with incomes of \$2,500 and over, who receive one-third of the total income available in this country, are the ones who have heretofore supported the private practice of obstetrics, and I cannot see why such a scheme as Dr. Daily's, directed at this lower income bracket, should affect private practice among upper income groups, who will doubtless want to continue with private practitioners.

Finally, let us consider the effect of this plan on individual enterprise and initiative. What rewards will this plan offer to the young man who is contemplating obstetrics and gynecology as a specialty? What rewards for intelligence, industry, originality of thought, research, surgical skill and executive ability? Any such scheme must provide such rewards, not only financial but academic rewards, for otherwise, our better young men will not be interested in entering the specialty. Of course, if that should happen, the program would be a toboggan which would carry us back to medieval midwifery. But I think that a plan can be worked out which does offer rewards to stimulate individual initiative.

The Society is to be congratulated on being able to hear this contribution of Dr. Daily. It is a subject which we must not get angry about, for it is a matter that deserves our dispassionate consideration. Surely, it is our responsibility to think very clearly about this whole problem and make certain that we reach conclusions that serve the best interests of both the mothers of our country and our specialty.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—Am I correctly under the impression that this Society is, consciously or unconsciously, engaged in a discussion of socialized medicine, or partly socialized medicine? If so, I must suggest that the matter is of such importance that it cannot be determined in a few hours. If it is the will of the Society that we should discuss the matter, it should be made the basis of an important symposium by the entire Society.

DR. CARL HENRY DAVIS, WILMINGTON, DEL.—I think I am one of the few who has had an opportunity to see something of medicine as it is practiced where all care is given by the government. I had the opportunity of visiting Russia in 1934 and 1935 when they were lessening the obstetric problem there by doing thousands of abortions every month. However, this was stopped in about 1936, and when I was there in 1937, the medical service of the government was having great difficulty in expanding its facilities rapidly enough to care for all pregnant women. Moscow was visited three times and I attempted to learn as much as possible about their medical practice. Their entire medical plan seemed to be worked out much like our teaching clinics. It is undoubtedly true that the average Russian receives much better medical care than he did formerly.

In the completely socialized state the doctor has a favored position. Professor Yudin, one of their foremost surgeons, received a salary of 25,000 rubles, which was many times the income of the average worker. He was on duty at the hospital a

specified period each day for five days and then he had a full day off. Free time was supposed to be used for research and study as well as recreation. This plan might have an appeal to those of us who have no control of our time.

Dr. Daily's plan to train 10,000 capable obstetricians would require many years and if patients demanded the services of individual men it might be impossible. One of our difficulties since the plan for the care of servicemen's wives has been the lack of hospital service cases for delivery by our interns.

Experience in large clinics suggests, however, that a considerable part of the population is interested in good service rather than the services of a certain doctor. It is my belief that obstetric care could be made less personal by having two or more men work together in such a way that only one would need to be on duty at the hospital during a night. The great mass of patients cannot pay for the type of services we as specialists try to furnish. Most of us could deliver several times as many patients each year if our deliveries could be accomplished in a manner which would lessen the number of disturbed nights. Skilled obstetric service for all will require radical changes from our present personal type of service. I think some plan should be worked out so that patients on a minimum pay basis could be delivered by an intern and have the obstetrician take care of them if there were complications.

DR. DAILY (closing).—The major purpose of presenting this paper was in order to bring to your attention what is really a serious problem today, and one which I think will confront us much more in the future. I hope all of you will be giving it a great deal of thought and attention. We should decide upon the objectives that we want; the methods of obtaining them are of secondary importance. If we can agree that we do want the best maternity care that can be provided in this country, for all mothers, I am sure that we can achieve it.

Department of Reviews and Abstracts

Review of New Books

Gynecology

Everett's *Gynecological and Obstetrical Urology*¹ is a single volume treatise devoted exclusively to urology of the female. At the Johns Hopkins Hospital, Howard Kelly's pioneer work with his direct vision cystoscope in the air-dilated bladder, and Hunner's observations on ureteral stricture and the elusive ulcer have influenced this school and are emphasized in this volume. The direct method of cystoscopy, which rarely is taught or used in other schools, is described in detail. This was the first method of cystoscopy that I learned, and although I now rarely use it, I can vouch, personally, to the simplicity and applicability of the direct method, but find that patients object to the posture. The various renal function tests are described. The indications for both intravenous and retrograde urography are outlined. For the excretory method, diodrast or neoiopep are recommended.

The cause of nongonorrheal chronic urethritis is ascribed to distant focal infections such as endocervicitis, trigonitis and ureteral stricture. The author emphasizes that with the advent of chemotherapy, the local treatment of cystitis by irrigation and instillation has decreased almost to the vanishing point. A very detailed description of interstitial cystitis—the "elusive" ulcer of Hunner—is given. Resection of the bladder for this lesion, has been abandoned; instead, strong topical applications are made to the small affected areas. Description of postradiation disturbances and lesions of the bladder is given. Vaginal cystotomy still is advocated for removal of vesical calculi which cannot be extracted through the cystoscope or cannot be crushed. The operation for simple stress incontinence consists of reefing the tissues at the bladder neck (Kelly's technique). In my experience, it is not possible to find adequate structures for this repair in every case as shown in Fig. 83 of the author. The treatment of vesical fistula, as well as that of ureteral fistula, is adequate. The various techniques for transplantation of the ureters into the bowel are described, including rectal implantation by the vaginal route.

Succeeding chapters deal with lesions of the kidney and ureter. Nephropexy for movable kidney producing symptoms is indicated in only about one-fourth of the patients. Ureteral stricture and multiform effects ascribed to it are detailed. The clinical forms of renal infection, tuberculosis of the urinary tract, calculous disease and tumors and trauma to kidney and ureter are fully described.

This urology of the female is lavishly and artistically illustrated. The reproduction of the x-ray films is unusually good. Chapter bibliographies are judiciously selected. This is a valuable contribution. The gynecologist and obstetri-

¹*Gynecological and Obstetrical Urology*. By Houston S. Everett, A.B., A.M., M.D., Associate Professor of Gynecology, the Johns Hopkins University and Associate in Gynecology, the University of Maryland. Assistant Visiting Gynecologist and Gynecologist in Charge of the Cystoscopic Clinic, the Johns Hopkins Hospital. Visiting Gynecologist, the Church Home and Hospital, the Hospital for the Women of Maryland and the Union Memorial Hospital. 517 pages. The Williams & Wilkins Company, Baltimore. 1944.

cian heretofore have been forced to wade through books on general urology, which focus chiefly on lesions in the male, in order to find scant references here and there to problems restricted to female patients.

R. T. FRANK.

Dr. Corner, who has previously written a book designed for the laity called the *Hormones in Human Reproduction*, has now written another volume, *Ourselves Unborn. An Embryologist's Essay on Man*² which appears as the twenty-first Terry Lecture. Usually a book designed for the laity, with very few exceptions, is an unpleasant chore for the reviewer. This certainly cannot be said for this volume which deals with embryology, particularly with human embryology. Dr. Corner has an uncanny talent for presenting in nontechnical terms the most difficult subjects. In this embryology, he gives the minutiae of this science, based on the huge Carnegie Institute collection, in a fully understandable fashion, and in such a way as to prove as absorbing and worth-while reading to the physician or medical student as to the lay reader. It requires a special talent to accomplish this difficult task. I have no hesitation in recommending this book to the profession as warmly as I do to the inquiring and educated layman.

R. T. FRANK.

A very logical publication arrangement brings two companion volumes on the subject of infertility which together consider the fertility of a couple rather than merely that of an individual. Siegler in his *Fertility in Women*³ discusses the causes, diagnosis, and treatment of impaired fertility in the female while Hotchkiss in his *Fertility in Men*⁴ discusses the same topics with regard to the male in the sterile mating.

In *Fertility in Women*, Siegler develops a logical perspective in his discussion of the subject. In his opening, and somewhat historical chapter, he makes the surprising statement that among Catholics the birth rate fell steadily from four offspring in a marriage in 1913 to two each in a marriage in 1920. Other racial and geographic factors are here evaluated.

The author's evaluation of fertility reveals its complex nature, and he discusses the various types of sterility, with a definite and methodical plan of investigation of sterile matings including the history, physical examination, and the marital relation. Proceeding to physiologic and functional development, there is a comprehensive discussion of the physiology of the female sex cycle. Particularly is this developed in relation to ovulation; the factors producing it, as well as the relation of ovulation to the various phases of the sexual act. Considerable space is devoted to the determination of the time of ovulation. Performances of various tests to determine the functional changes of the menstrual cycle are detailed and illustrated. The author assumes from the many investigations of his own and others that ovulation may occur at any period in the cycle, but particularly from the eighth to twentieth day. He feels that the simple procedures of proved value are sufficient to determine ovulation and may be checked, when necessary, by endometrial biopsy and hormonal assays. In the third part of the book he takes up treatment, discussing the factors and the

²*Ourselves Unborn. An Embryologist's Essay on Man.* By George W. Corner. 188 pages. Yale University Press, New Haven. 1944.

³*Fertility in Women.* By Samuel L. Siegler, M.D., F.A.C.S. Attending Obstetrician and Gynecologist, Brooklyn Women's Hospital; Attending Gynecologist, Unity Hospital. With a Foreword by Robert L. Dickinson, M.D. 194 illustrations including 40 subjects in full color on 7 plates. J. B. Lippincott Company, Philadelphia, London, and Montreal. 1944.

⁴*Fertility in Men.* By Robert S. Hotchkiss, B.S., M.D. Lieutenant Commander (MC) USNR (on active service), Asst. Prof. of Urology New York University Medical College. With a Foreword by Nicholson J. Eastman, M.D. 95 illustrations. J. B. Lippincott Company, Philadelphia, London, and Montreal. 1944.

methods which may be used to overcome infertility. He states in this discussion that relief of sterility by hormonal therapy was found to be variable, unpredictable and disappointing. The surgical therapy of conditions accounting for faulty reception of spermatozoa is discussed. It is interesting to note that the author had four, of twenty-three patients operated upon for tubal occlusions, conceive and deliver at term. One feels that the author is opposed to artificial insemination; he states that very few sterile couples qualify for it.

In the companion volume, *Fertility in Men*, Hotchkiss discusses the subject of infertility from the male standpoint. Particularly valuable is the opening chapter regarding past prejudices on the part of the male and suggestions as to the physician's approach to this phase of the question. The author discusses the anatomy and physiology of the male genital organs, and describes the various pathologic lesions which may influence the function of the testes and other elements of the male generative tract.

A comprehensive picture of the metabolism and composition of the semen is given. Under clinical inferences, the author discusses the relationship of the female genital secretions as they are related to the welfare of the sperm. This question is also taken up by Siegler in his book, and apparently this relationship forms one of the still unsolved questions of infertility.

Several succeeding chapters are devoted to the methods of appraising fertility in men, which include laboratory analyses, cell counts and morphology with a discussion of the variabilities of semen and the factors which influence their characteristics.

Dr. Hotchkiss closes this book with a very rational consideration of the problems of treatment, and he has made a final chapter of unusual value by including case histories to illustrate effects of treatment in the deviations of semen, volume, motility, number, percentage of abnormals, usually encountered. The text is clear and concise and emphasis has been placed on the practical details.

These companion volumes are highly recommended to all those who are interested in any part of the subject of infertility since they offer a fine working guide to the problems of a couple so troubled.

PHILIP F. WILLIAMS.

A second edition of *Novak's Textbook of Gynecology* has appeared after an interval of three years. The text has been enlarged by more than one hundred pages, and forty additional illustrations. The title of the book has been shortened from *Gynecology and Female Endocrinology* to a *Textbook of Gynecology*.

The revision has been thorough. Two new chapters have been added. The embryology is largely based on the slides loaned by Dr. Robert Meyer. The description of the formation of the vagina is particularly adequate, and the illustrations are interesting. The final chapter, written by H. S. Everett deals with the common disorders of the female urinary organs. It covers the ground adequately. The treatment of gonorrhea is to be commended because the main treatment now consists of sulfa therapy with entire omission of local treatment during the acute stages. It might have been mentioned that the small number of sulfa resistant cases, particularly the chronic ones, can be cured by means of penicillin.

Throughout the text, Gartner's duct, etc., is "Gärtner's." August Gärtner was a German bacteriologist after whom the Gärtner's bacillus, a member of the salmonella group was named; Herman T. Gartner was a Danish anatomist who described the residue of the Wolffian duct found in the female.

Textbook of Gynecology. By Emil Novak, M.D., F.A.C.S. Associate in Gynecology, The Johns Hopkins Medical School; Gynecologist, Bon Secour and St. Agnes Hospitals, Baltimore. Second Edition. 769 pages. The Williams and Wilkins Company, Baltimore. 1944.

Novak's Gynecology is a very readable textbook which covers the ground thoroughly. The author has the ability to describe conditions clearly and particularly to correlate, clarify and epitomize the enormous amount of material which has accumulated. Short bibliographies are found at the end of each chapter.

R. T. FRANK.

Peel has undertaken the task of revising and enlarging a **Textbook of Gynaecology** by Forsdike.⁶ Judged by American standards the book approaches an ample compend rather than a textbook. The chapters on physiology and hormonal control are clear and up to date. The clinical conditions are tersely and well presented. The treatment advised is conservative.

The illustrations of gross specimens are good and numerous. The drawings of microscopic specimens are quite schematic, the photomicrographs are better. An appendix containing "endocrine products available in Great Britain and the Colonies" contains a long list of biologically tested pharmaceuticals with names foreign and unknown in the United States. For the student studying in this country the book has little to offer.

R. T. FRANK.

History of Gynecology by Leonardo⁷ has a foreword by Greenhill and a second one by Victor Robinson. The subject is covered in twenty-eight chapters, and takes in the usual history of ancient medicine beginning with the Egyptians and the middle ages, the gynecology of the Renaissance, and those of succeeding centuries.

To me the most interesting chapter is that on recent advances in which the author covers the development of gynecology in the last one hundred and fifty years very briefly, but containing a great deal of worth-while material. The book is well written and makes pleasant reading. There is a bibliography at the conclusion, and both a subject and authors' index which make reference easy.

R. T. FRANK.

The third edition of **Gynecological Therapy** by Calatroni and Ruiz⁸ to appear since 1938, is a huge tome of 1212 pages, 38 chapters, with 442 illustrations. It has been brought up to date by incorporating into the text our newer knowledge on sulfa therapy, androgen therapy and discussion of the possible carcinogenic effect of prolonged use of estrogens. A new chapter on nonvenereal skin lesions of the vulva has been contributed by Quiroga. The chapter on neuropsychiatry is by Thenon.

The encyclopedic contents of this volume preclude an attempt at detailed review. Every field of gynecology including the allied gynecologic endocrinology and radiotherapy are covered. Particular attention is given to functional disturbances. Cancer as well as benign lesions are dealt with.

True to the title, therapy is the main theme, described in detail and often embracing remedies, which have been abandoned in this country. Operative tech-

⁶**Forsdike's Textbook of Gynaecology.** Revised, enlarged and in part rewritten by J. H. Peel, M.A., B.M., B.Ch. (Oxon.), F.R.C.S., M.R.C.O.G., Assistant Obstetric and Gynaecological Surgeon, King's College Hospital and Princess Beatrice Hospital, etc. 440 pages. Grune and Stratton, New York. 1944.

⁷**History of Gynecology.** By Richard A. Leonardo, M.D., Ch.M., F.I.C.S. Fellow Royal Society of Medicine (London); Fellow American Medical Association; Fellow International College of Surgeons, etc. Forewords by Prof. J. P. Greenhill (Loyola University) and Prof. Victor Robinson (Temple University). 434 pages. Froben Press, New York. 1944.

⁸**Terapeutica Ginecologica.** Por Carlos J. Calatroni, Docente Libre de Clínica Ginecológica (Buenos Aires), Jefe de Trabajos prácticos de la Cátedra and Vincente Ruiz, Professor Titular de Clínica Ginecológica (La Plata), Docente Libre de Clínica Ginecológica (Buenos Aires) III Edición. 1212 pages. Ferrari Hnos. Buenos Aires. 1944.

niques are outlined, frequently also illustrated. Each chapter is followed by an ample formulary of prescriptions. Liberal, but on the whole conservative, use of endocrine therapy is advocated. According to the authors no substantiated proof of carcinogenesis in the human being due to the use of estrogens, has been demonstrated. Androgen therapy is limited by its high cost and the dangers of masculinization.

The book is lavishly and effectively illustrated. Due credit is given to authors when their illustrations are used. On the other hand, in this large volume there is no bibliography and no index.

R. T. FRANK.

Proceedings of the Conference on Problems of Human Fertility edited by Engle⁹ gives a detailed account of the meeting held in 1943, under the auspices of the National Committee on Maternal Health. Three topics were discussed—criteria of ovulation, some biological observations on the lower generative tract, and in what fashion the placenta acts as a barrier between mother and child. These fundamental questions were dealt with by a number of well-known investigators. It is impossible to single out individual articles for review. The aspects covered were endocrine, embryological, histological, chemical as well as physiological. The material is presented in a very compact way and in each instance followed by a discussion by members of the conference. A huge amount of information is given, information much of which has not yet reached publication.

R. T. FRANK.

Obstetrics

In this historical review *Hydronephrosis and Pyelitis of Pregnancy*¹⁰ Dr. Robertson documents 974 references. The facts and theories presented in these articles and the deductions which he has drawn from them are presented in a series of fourteen chapters, which in discussing the etiology and pathogenesis of the two subjects under consideration brings out the anatomic relations, bacteriology, nervous chemical and nutritional influences. There are also chapters on eclampsia, intravenous urography and the end results of hydronephrosis and pyelitis in pregnancy. He summarizes the material in the chapter entitled "Discussion" after which he enumerates the conclusions which may be drawn from his historical review.

Robertson feels that if the dilatation of the ureter in pregnancy is abnormal enough to constitute a real disease, and this is his attitude, then measures for its prevention as well as avoidance of its more dangerous complications should be instituted. He regards hormonal influences and chemical and nutritional disturbances as minor effects. Infection, pyelitis and pyelonephritis are regarded as subsequent to stasis. The author feels that every inflammation of the renal or urinary pelvis is accompanied by inflammation of the renal substance. He is skeptical about primary pathogenicity of *B. coli*. He argues against the hematogenous route and feels that most inflammatory lesions are due to pathogenic bacteria which regularly inhabit the urogenital regions.

Regarding the prognosis he suggests postpuerperal intravenous urographic studies. Space has not permitted him to discuss the relationship of pyelitis to the fetus,

⁹*Proceedings of The Conference on Problems of Human Fertility*. Sponsored by the National Committee on Maternal Health, January 15 to 16, 1943, New York City. Edited by Earl T. Engle. 182 pages. Published for the National Committee on Maternal Health by George Banta Publishing Company, Menasha, Wisconsin. 1943.

¹⁰*Hydronephrosis and Pyelitis (Pyelonephritis) of Pregnancy: Etiology and Pathogenesis. An Historical Review*. By H. E. Robertson, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minn. Pp: 319. W. B. Saunders Company, Philadelphia, 1944.

interruption of pregnancy, or immediate life expectancy of the mother. Surgery he states should be undertaken as a last resort, and he advises no succeeding pregnancy if any evidence of infection persists. This review is an excellent recapitulation of the history and present-day facts on these urological entities.

PHILIP F. WILLIAMS.

Weisman and Coates have written a complete monograph on *The South African Frog (Xenopus Laevis) in Pregnancy Diagnosis*.¹¹ This covers the subject very completely, including the discovery of this animal, its habitat, anatomy, behavior, reproduction, etc. The African frog was first used for pregnancy tests in South Africa, then taken up by Crew of Edinburgh, and introduced into this country by Weisman. Apparently, the frog has been used extensively now by others. As a test object, the accuracy compares with both the original Aschheim-Zondek and the Friedman tests.

To those unfamiliar with this test, it should be mentioned that the same frog, if given a vacation of four weeks, can be used many times. However, according to Weisman's technique, eight frogs which would be sufficient for four tests, require three tanks of twelve gallons each in order to have a stock, a preparatory, and a recovery tank. The authors use, except in advanced pregnancy, a concentration of urine, precipitating 80 c.c. of urine with twice the amount of acetone. The precipitate either obtained by decantation or centrifuged is then allowed to dry and is taken up in 2 c.c. or more of distilled water. An alternative method after precipitation is to filter, and adjusted to a pH of 5.5. The animal is injected in its dorsal lymph space, with the equivalent of 40 c.c. of urine, and then placed in a small test tank containing a one-half inch mesh screen, a small distance from the bottom of the tank, through which the extruded eggs drop. The animals are examined every four hours. If, after eighteen hours, no eggs are visible, the test is considered negative. Animals which react negatively may be used again in three to seven days.

In reading this monograph it becomes apparent that considerable care in keeping these animals is required. Their present cost, at retail, is ten dollars each.

R. T. FRANK.

In *Caesarean Section, The History and Development of the Operation From Earliest Times*¹² which Dr. Young submitted as a graduation thesis of the University of Edinburgh in 1942, one finds a very complete history of this procedure. He has delved deeply into the origin of the name of the operation and its early performances. He divides his story of the development of this operation into three periods: that prior to 1500, the second period from 1500, when the first authenticated operation of cesarean section was performed on a living woman, and the third period from 1876, which year marks the beginning of the development of the modern technique of the operation following the work of Porro and Sanger.

In the first section, the author has reviewed the literature of the time with extensive quotations from the records of those days. It would seem that most of the operations performed in that period were emergencies with high mortality.

¹¹*The South African Frog (Xenopus Laevis) in Pregnancy Diagnosis*. A Research Bulletin. By Abner I. Weisman, M.D., Adjunct Gynecologist, Jewish Memorial Hospital; Assistant Visiting Gynecologist and Obstetrician, Metropolitan Hospital, New York, N. Y. and Christopher W. Coates, Aquarist, New York Zoological Society, Research Associate to the Department of Pathology, Jewish Memorial Hospital, New York, N. Y. Aided by a grant from the New York Biologic Research Foundation. 1944.

¹²*Caesarean Section: The History and Development of the Operation From Earliest Times*. By J. H. Young, M.B., Ch.B. Pp:224. H. K. Lewis and Co. Ltd., London, 1944.

In the second period up to the introduction of the Porro operation, the terrible mortality produced a tremendous debate on the relative merits of cesarean section and craniotomy. Nevertheless, as the author shows, the operation was increasingly performed in various countries.

The more successful results obtained by the technique of Porro, led to development of the classical operation and the seroseros approximation of the uterine wound popularized by Sanger. After recounting the ever broadening modern indications for cesarean section, the author relates the efforts to popularize cesarean section in placenta previa. He describes the efforts to avoid infection and in the more recent attempts to reach the uterus extraperitoneally.

The author has given us a fine recital of the origin of this operation and of the stages through which its evolution has come. The work is well documented and the quotations from writings difficult to obtain are usually full. The book should be of interest to those interested in the origin as well as the present place of the operation in obstetric practice.

PHILIP F. WILLIAMS.

The last issue of *Dr. Greenhill's Year Book* (1943)¹³ is again replete with a valuable review of the annual progress in this field of medicine. The abstracts from the literature are complete and supplemented by valuable editorial comments as well as a most satisfactory index. The principal topics dealt with include the use of the sulfa group of drugs, caudal anesthesia, vaginal infestations, clinical pelvimetry, progesterone treatment of abortion, androgen therapy, hemorrhagic disease in the newborn, endometrial biopsies, treatment of obstetric hemorrhages, etc. Notwithstanding the absence of references to the foreign literature, there is no apparent reduction in the size of the present volume, which demonstrates the extent of the activity of American authors. Greenhill's work constitutes an invaluable source of information for the practitioner as well as the specialist in obstetrics and gynecology.

GEO. W. KOSMAK.

Dr. Read in his *Childbirth Without Fear*¹⁴ again stresses the significance of emotional factors on the reproductive functions of women to which he first called attention in 1933 in the book *Natural Childbirth*.

He regards pain, fear, and tension as a syndrome which is responsible for the pain of labor, and explains the various factors which predispose to a low threshold of pain interpretation and which may be regarded as subject to correction. In discussing the factor of fear, he analyzes this emotion in relation to mental imagery, and brings out the point that fear of childbirth is becoming a conditioned reflex bringing about the idea of pain and its associated tension.

He feels that a thorough explanation in early pregnancy to the patient of the physiology of parturition and the various phenomenon of labor would do much to dispel the fear factor as a conditioning reflex. He explains thoroughly the type of education employed both in pregnancy and at the beginning of labor, as carried out in his own practice to the point where anesthesia is seldom, if ever, needed. His application of the practice of relaxation in obstetrics, the therapeutic method developed by Jacobson, brings about, apparently, a lessening of the tension factor. He details instruction on the method by which such relaxation may be obtained.

¹³The 1943 Year Book of Obstetrics and Gynecology. By J. P. Greenhill, M.D., Chicago, The Year Book Publishers, Inc. 1944 p. 554. Price, \$2.00.

¹⁴Childbirth Without Fear. The Principles and Practice of Natural Childbirth. By Grantly Dick Read, M.A., M.D. Pp: 257. Harper and Brothers. New York and London. 1944.

Since American women have been so sold, by lay publications, on the idea that parturition is an exceedingly painful process, it is to be doubted whether a widespread adoption by obstetricians of Read's technique would bring about childbirth without fear earlier than within a period of several generations.

PHILIP F. WILLIAMS.

Special Delivery by Rosenberg¹⁵ is a handbook for expectant mothers. In a clear, understandable way, the anatomy of the pelvis, the mechanism of labor, the changes in the puerperium, in fact the entire process of delivery, including the anesthesia, forceps, etc., are given. This little manual is well illustrated. Its purpose is to dispel in the most effective way the phobias entertained by pregnant women. Whether even this nicely presented description will actually serve its purpose must be considered doubtful. There is no question that an intelligent, well-poised and well-balanced woman may derive distinct benefit from such knowledge. On the other hand, the fearsome neurasthenic may very well react in quite the opposite way.

R. T. FRANK.

The thirteenth edition of **DeLee's Obstetrics for Nurses**¹⁶ appears under the authorship of M. Edward Davis, M.D., and Mabel C. Carmon, R.N., who have succeeded the late Doctor DeLee. The book has been reorganized on the unit basis to bring it in line with the recommendations of the curriculum guide of schools of nursing. The authors are fortunate to have had the assistance of many able leaders in the obstetric and nursing field in preparing various sections of the book, and the criticisms of those who are actively engaged in obstetric nursing. Specifically, one may mention the excellent new section entitled, "The Reasons for Failure of the Fetus or Young Infant to Survive," which particularly emphasizes the points brought out in an earlier section in the fifth unit in nursing in the neonatal period.

PHILIP F. WILLIAMS.

Thirty Cases of Puerperal Infection by de Carvalho¹⁷ is a brief monograph, detailing thirteen of the case histories. The value and dangers of the sulfa drugs are discussed.

Miscellaneous

In this book, **Pain Mechanisms**¹⁸ Dr. Livingston discusses the clinical aspects of pain, especially the study and interpretation of the clinical syndrome which may develop following nerve injury and which is designated as "causalgia." He acknowledges the complexities of the problems regarding pain, and the difficulty of presenting the results of clinical observations and of physiological investigation in a manner at once acceptable to research workers as well as to the

¹⁵**Special Delivery. The Expectant Mothers' Handbook.** By B. D. Rosenberg, M.D. With illustrations by Gladys McHugh. 96 pages. Ziff-David Publishing Company, New York. 1944.

¹⁶**DeLee's Obstetrics for Nurses.** By M. Edward David, M.D., Professor of Obstetrics and Gynecology, University of Chicago and Mabel C. Carmon, R.N., Chief Supervisor and Instructor in the Birthrooms, Chicago Lying-in Hospital and Dispensary. Thirteenth Edition, Reset. Pp: 575. Ill. 306. W. B. Saunders Company, Philadelphia and London, 1944.

¹⁷**Trinta Casos de Infecções Puerperais.** By J. Coriolano de Carvalho, Premio Alvarenga da Faculdade Nacional de Medicina. 40 pages. Trabalho apresentado e discutido na 11 Semana Paulista-Carioca de Ginecologia e Obstetrica, de Setembro de 1943. Rio de Janeiro. 1943.

¹⁸**Pain Mechanisms. A Physiologic Interpretation of Causalgia and Its Related States.** By W. K. Livingston, Lieutenant Commander, (MC), USNR. Pp: 248. The Macmillan Company, New York, 1943.

clinicians. The material deals, first, with the physiology and psychology of pain; second, with the clinical aspects, and finally, with the interpretation. Some chapters of the book, chronic low back disability, the sympathetic component, and the vicious circle, would be of interest to many gynecologists as an aid in the solution of some traumatic or sympathetic system disorders, which not infrequently, appear in their practices. To the surgeon or neuropsychiatrist who will handle many cases of this type after the war, this book should be of much value.

PHILIP F. WILLIAMS.

After eight years, a second translation of Hermann Zondek's *The Diseases of the Endocrine Glands* by Carl Prausnitz Giles,¹⁹ a translation of the fourth German edition, has appeared. This is a book based upon a large clinical experience, deeply tinged by the author's personal views, often therefore interesting and illuminating, but sometimes distinctly hypothetical. The book is designed for clinicians.

The introductory chapters dealing with the physiology of the hormones and the individual glands are very clear, detailed and informative. The chapters on diseases of the thyroid are good; those describing the pituitary disturbances are excellent. Obesity is gone into fully. On the other hand, only ten pages are devoted to adrenal diseases and hyperinsulinism is given only five pages. Diabetes has not been included. Most of the remainder of the volume is devoted to disorders of the generative system—both male and female—considered from many aspects, including their effect on tumor formation, blood, etc. Therapy is described in great detail and without undue overoptimism. The illustrations are numerous and original. The translation is excellent and smooth.

R. T. FRANK.

According to the publisher's preface, *Sexual Anomalies*²⁰ was written by the pupils of Magnus Hirschfeld, based upon his notes as well as his published papers. Hirschfeld had planned to write this book himself. The names of none of these pupils appear in the volume. The book is designed for those whose professional duties require a knowledge of sexual pathology—physicians, criminologists, attorneys, judges, probation officers and educators.

In the early years of this century, Hirschfeld played a dominant role in this field throughout the Germanic countries. He founded and endowed an institute for Sexualwissenschaft in Berlin, and then presented it to the German people. With the advent of the Nazis, the institute was discontinued, the author's books publicly burned, as well as his notes and huge number of case histories.

In the present textbook, Hirschfeld and his pupils have essayed to combine the developmental, hormonal and Freudian theories in a concise, readable form. The main bulk of the volume consists of numerous case histories.

R. T. FRANK.

¹⁹*The Diseases of the Endocrine Glands.* By Hermann Zondek, M.D. (Berlin). Director of the Medical Division, Bikur Cholim Hospital, Jerusalem; Late Extraordinary Professor of Medicine in the University of Berlin and Director of the Medical Division of the Krankenhaus am Urban in Berlin; Late Honorary Physician to the Victoria Memorial Jewish Hospital, Manchester. Fourth (Second English) Edition. Translated by Carl Prausnitz Giles, M.D. (Breslau), M.R.C.S. (Eng.), L.U.C.P. (Lond.). Late Honorary Professor of Medicine, Victoria University of Manchester; Late Professor of Hygiene and Bacteriology, University of Breslau. 496 pages. Williams & Wilkins Company, Baltimore. 1944.

²⁰*Sexual Anomalies and Perversions. Physical and Psychological Development and Treatment. A Summary of the Works of the Late Professor Dr. Magnus Hirschfeld, President of the World League for Sexual Reform, Director of the Institute for Sexual Research, Berlin, etc. Compiled as a Humble Memorial by his Pupils.* 636 pages. Francis Alder Publisher, London, England. Emerson Books, Inc., New York. 1944.

From its initial chapter on historical consideration, to the concluding, very timely chapter on *Intravenous Anesthesia*,²¹ in *Military Surgery*, this monograph discusses exhaustively a technique which is assuming increasing importance in the field of anesthesiology and surgery. Individual chapters are allotted to all the drugs that have been employed for anesthesia by this method. Following a historical survey, the chemistry, pharmacology, clinical use, indications and contraindications for administration of these agents, are discussed in detail. A complete bibliography is included in each chapter. The technique of administration is described thoroughly by the text and by numerous illustrations.

Special consideration is given to pentothal sodium, which to the present time, has proved to be the most satisfactory drug for intravenous anesthesia. The author's very extensive personal experience in the use of this drug makes this chapter particularly valuable. This is an informative book for the anesthetist student and research worker.

BERNARD H. ELIASBERG.

This volume *The Art of Anesthesia*²² carries but very inconsequential changes in the text of the previous edition. There has been added a chapter on Fire Hazard in Anesthesia, a chapter on Our Wives and Children—Who Shall Anesthetize Them? a very short chapter on Continuous Spinal Anesthesia, and a concluding, very brief chapter on Continuous Caudal Anesthesia in Obstetrics. Its popularity is attested to by the fact that it has undergone seven editions.

BERNARD H. ELIASBERG.

The fifth edition of *Hewer's Recent Advances in Anaesthesia and Analgesia*²³ has appeared in twelve years. This is not surprising because the book contains a large amount of information in small compass.

In spite of the pressure of war, research in anesthesia has not lagged, in fact it has been stimulated in certain fields. The new edition contains additions on anesthesia for thymectomy (myasthenia gravis), intravenous general analgesia with ethyl chloride, trichlorethylene and procaine, analgesia in obstetrics, fractional caudal block, etc. Concise chapter bibliographies and liberal illustrations add to the value and readability of the book.

R. T. FRANK.

Minor Surgery,²⁴ edited by Rolleston and Moncrieff, contains eighteen contributions by as many authors on diverse subjects—minor wounds, sprains, the feet, the hand, the mouth, the nose and throat, the ear, the eye, bursae and ganglia, some benign tumors and cysts, skin infections, the rectum, the genitourinary system, nonoperative treatment of hernia, varicose veins, ulcers and phlebitis, gynecology, childhood, and anesthesia and analgesia.

There is no preface or introduction, but from the text one gathers the impression that this small volume is designed for ready reference especially for the

²¹*Intravenous Anesthesia*. By R. Charles Adams, M.D., C.M., M.S., Associate in Section on Anesthesiology, Mayo Clinic, Rochester, Minn. Cloth. Pp. 663, with 75 illustrations. New York and London. Paul B. Hoeber, Inc., 1944.

²²*The Art of Anesthesia*. By Paluel J. Flagg, M.D. Visiting Anesthetist to Manhattan Eye and Ear Hospital, New York City. Seventh Edition. Cloth. Pp. 519, with 166 illustrations, and foreword by Dr. Rudolph Matas. Philadelphia. J. B. Lippincott Co. 1944.

²³*Recent Advances in Anaesthesia and Analgesia (Including Oxygen Therapy)* by C. Langton Hewer, M.D., B.S. (Lond.), D.A. (Eng.). Senior Anaesthetist, St. Bartholomew's Hospital and St. Andrew's Hospital, Dollis Hill; Anaesthetist, Brompton Chest Hospital and Emergency Medical Service, etc. Fifth Edition with 141 illustrations. 343 pages. The Blakiston Company, Philadelphia. 1944.

²⁴*Minor Surgery*. Edited by Humphry Rolleston and Alan Moncrieff. 174 pages. Philosophical Library, New York. 1944.

practitioner, who must be prepared to cope with all situations often under wartime conditions. However, the content is not limited to acute or traumatic disturbances.

For disinfection of minor wounds Dettol is recommended. Varicose veins are injected with quinine and urethane. The chapter on gynecology was contributed by Douglas MacLeod. It includes Bartholinian conditions, urethral caruncle, episiotomy, perineal and vaginal lacerations, cervical polyps, trachelorrhaphy, amputation of the cervix, cervical dilatation, curettage, insufflation and visualization of the tubes. That the advice is designed for action under wartime conditions is evidenced by the advice for treatment of complete perineal tears—"Should the delivery occur at night, it is wise to wait until the following day in order to have sufficient light and assistance at its performance."

The text is concise and authoritative.

R. T. FRANK.

A monograph by Ribeiro on **Lithiasis of the Appendix**²⁵ contrasts the frequency of coproliths and the rarity of true appendicular stone. A coprolith is a fecal concretion; a stone usually consists of a fecal core about which mineral salts have formed layers. During its formation stones remain clinically quiescent, but eventually may produce an acute appendicitis.

The author reports one case, the appendix containing four stones. Complete literature.

R. T. FRANK.

Chronology of the Evolution of Plastic Surgery²⁶ is in the nature of a prospectus of a book to appear next year by the same author and publishers, a chronology which covers the periods from the first century B.C. to 1944, in the form of a thirty-two-page pamphlet. It begins with the Chinese tannic acid treatment of burns five thousand years B.C., and ends with an osteoplastic procedure for funnel chest. For quick reference it might be of value.

R. T. FRANK.

This book²⁷ represents, in large part, a summary of the studies made by these authors in hypertensive diseases by measurements of the effective renal blood flow, filtration rate and maximal tubular excretory capacity with the diodrast and inulin methods devised by Homer Smith. There are excellent chapters on the clinical aspects of hypertensive diseases, on systemic hemodynamic alterations in hypertension, and renal functional and renal hemodynamic alterations in hypertension. They repeat the often quoted statement that "the cause of essential hypertension is unknown." While this is true as far as the precise mechanism is concerned, one cannot ignore the abundant accumulated evidence of the psychogenic origin of essential hypertension. Indeed, the authors emphasize the value of psychotherapy in the therapy, but aside from this brief comment there is no

²⁵*Litíase do Apêndice*. By Eurico Branco Ribeiro, Director Do Sanatório São Lucas. 87 pages. Sociedade Editora Médica Limitada, São Paulo, Brazil. 1943.

²⁶*Chronology of the Evolution of Plastic Surgery*. By Maxwell Maltz, B.S., M.D., Sc.D., F.I.C.S.; Director, Department of Plastic and Reconstructive Surgery, West Side Hospital and Dispensary; Honorary Professor of Surgery, Universities of Santo Domingo, Nicaragua, Honduras, San Salvador, Guatemala, etc. This Chronology is a section from the author's volume: *The Evolution of Plastic Surgery* (Froben Press, 1945). 32 Pages. Froben Press, New York. 1944.

²⁷*Hypertension and Hypertensive Disease*. By William Goldring, Associate Professor of Medicine, New York University College of Medicine; Chief, Nephritis and Hypertension Clinic, New York University Clinic; Physician to the Adult Cardiac Clinic and Associate Visiting Physician, Third (New York University) Medical Division, Bellevue Hospital; Visiting Physician, Goldwater Memorial Hospital, and Herbert Chasis, Assistant Professor of Medicine, New York University College of Medicine; Associate Chief, Nephritis and Hypertension Clinic, New York University Clinic; Physician to the Adult Cardiac Clinic and Assistant Visiting Physician, Third (New York University) Medical Division, Bellevue Hospital; Cardiologist to the French Hospital, New York, The Commonwealth Fund, 1944.

discussion of this important phase of the etiology of essential hypertension. They conclude that the results attained by experimental hypertension cannot be applied to human hypertension except to a very limited degree, and that there is no proof that essential hypertension is of primary renal origin. They are skeptical of the reports of the cure of hypertension by unilateral nephrectomy. There are two long chapters on therapy of hypertensive disease. They do not approve of the thiocyanate treatment and conclude that renal extracts have thus far been unsuccessful in the treatment of hypertension. The principal effect of sympathectomy is the relief of subjective symptoms, and the occasional temporary reduction of blood pressure to lower levels.

The work concludes with several appendices on methodology of blood pressure measurement with the direct method; cardiac output measurement; peripheral resistance; the rate of glomerular filtration, effective renal plasma flow, maximal tubular excretory capacity, maximal tubular resorptive capacity; composite kidney function test, functional and hemodynamic measurements of separate kidneys and a presentation and discussion of renal functional data in hypertensive patients. One misses a chapter on the anatomical aspects of hypertension. The authors omitted it because these may be found in other books, but this argument may be applied to a large part of the text of this volume; a clear perspective of hypertensive disease can hardly be gained without including a background in morbid anatomy. Within its scope, this book is excellent and informative.

ELI MOSCHCOWITZ.

The Twentieth Edition of Dorland's Medical Dictionary²⁸ covers every department of medicine and surgery and the allied fields. The many additions and alterations required to meet recent advances have necessitated a complete revision of previous editions. The *Standard Nomenclature of Diseases and Operations* has been used as the basis of terminology and constitutes a notable feature. Attention may also be called to the gallery of portraits of eminent medical men and their principal association with accepted terms. Perhaps in later editions, the insertion of a few more biographic details might be considered. The various tabulations are also of importance. The collaboration of Dr. E. C. L. Miller, well-known librarian of the Medical College of Virginia, is an important addition to the list of other competent authorities in their respective fields, making this new edition the outstanding work of reference in American medical literature.

GEORGE W. KOSMAK.

This Golden Book²⁹ is an anniversary volume dedicated to Professor Osvaldo L. Bottaro upon the completion of thirty years of professorship including his gynecologic service at the Hospital San Roque (1912-____). The recipient of this honor has published over many years diverse subjects in gynecology and obstetrics, as well as on public health problems.

The content of this faultlessly gotten up volume of nearly five hundred pages does not lend itself to detailed review as it embraces every aspect of medicine including such diverse subjects, selected at random, as the medical, ethical and professional aspects of female sterility, the treatment of tuberculous cavities, postoperative exophthalmos in Basedow's disease, recent advances in the therapy of mental diseases, in addition to a number of strictly gynecologic themes.

R. T. FRANK.

²⁸The American Illustrated Medical Dictionary. By W. A. Newman Dorland, A.M., M.D., F.A.C.S., Twentieth Edition. Revised and Enlarged. With the Collaboration of E. C. L. Miller, M.D., Philadelphia and London, W. B. Saunders Co., 1944. 1668 pages. Price \$7.00, thumb-indexed, \$7.50.

²⁹Libro de Oro. Ofrecido Al Professor Honorario Dr. Osvaldo L. Bottaro. Al Cumplir 30 Años en el Ejercicio Del Profesorado por sus Discípulos, Colaboradores y Amigos. 493 pages. Alfredo Frascoli, Buenos Aires. 1943.

Item

American Board of Obstetrics and Gynecology

Examination

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 3, 1945, at 2:00 P.M.

Arrangements will be made so far as is possible for candidates in Military Service to take the Part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the Commanding Officer (medical) or some responsible person designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Candidates for the February 3, 1945, Part I examination, who are entering Military Service, or who are now in Service and may be assigned to foreign duty, may submit their case records in advance of the above date, by forwarding the records to the Office of the Board Secretary. All other candidates should present their case records to the examiner at the time and place of taking the written examination.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

All candidates will be required to take both the Part I examination, and the Part II examination (oral-clinical and pathology examination). Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held later in the year.

Notice of the exact time and place of the Part II examinations will be sent all candidates well in advance of the examination date. Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

If a candidate in Service finds it impossible to proceed with the examinations of the Board, deferment without time penalty will be granted under a waiver of our published regulations applying to civilian candidates.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS.

Necrology

Elijah White Titus

Elijah White Titus, M.D., a graduate of George Washington University, in 1910, Clinical Professor in Obstetrics and Gynecology in the latter, Attending Gynecologist in the Columbia Hospital for Women and the George Washington University Hospital, Fellow of the American College of Surgeons, Past President of the Washington Medical Society, a diplomate of the Board of Obstetrics and Gynecology, died at his home, in Washington, D. C., December 11, 1944, after a brief illness.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

- American Gynecological Society.** (1876) *President*, Edward A. Schumann, Philadelphia, Pa. *Secretary*, Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** (1888) *President*, Lewis F. Smead, Toledo, Ohio. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.
- Central Association of Obstetricians and Gynecologists.** (1929) *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Dallas, Tex. Annual meeting not announced.
- South Atlantic Association of Obstetricians and Gynecologists.** (1938) *President* Oren Moore, Charlotte, N. C. *Secretary*, T. J. Williams, University, Va. Annual meeting cancelled.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas Tex. Next meeting, Philadelphia, Pa., June 18-22, 1945.
- New York Obstetrical Society.** (1863) *President*, W. E. Studdiford. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** (1868) *President*, Charles A. Behney. *Secretary*, John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** (1878) *President*, William J. Dieckmann. *Secretary*, Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** (1890) *President* Chas W. Mueller. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society.** *President*, Edward Friedman. *Secretary*, Carroll J. Fair, Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Howard Stearns. *Secretary*, William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** (1934) *President*, H. A. Power. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** (1861) *President*, Thos. Almy, Fall River, Mass. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

- New England Obstetrical and Gynecological Society.** (1929) *President*, Roy J. Hefferman, Brookline, Mass. *Secretary*, Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society.** (1931) *President*, T. Floyd Bell. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society.** (1933) *President*, James R. Costello. *Secretary*, J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.
- New Orleans Obstetrical and Gynecological Society.** (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society.** (1924) *President*, S. A. Weintraub. *Secretary*, Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society.** (1929) *President*, R. Glenn Craig. *Secretary*, D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists.** (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists.** (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Norman F. Miller. *Secretary*, Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Obstetric Society of Syracuse Hospitals.** (1938) *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.
- Alabama Association of Obstetricians and Gynecologists.** *President*, J. M. Weldon, Mobile, Ala. *Secretary*, Eva F. Dodge, Montgomery, Ala.
- San Antonio Obstetric Society.** *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society.** (1941) *President*, R. Philip Smith. *Secretary*, Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings held on third Wednesday of each month.
- Denver Obstetrical and Gynecological Society.** (1942) *Secretary*, Emmett A. Mechler, 1612 Tremont St., Denver, Colo. Suspended during war.
- Wisconsin Society of Obstetrics and Gynecology.** (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society.** (1937) *President*, Geo. D. Huff. *Secretary*, Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology.** (1938) *President*, Ralph E. Leigh, Grand Forks. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society.** (1936) *President*, A. L. Carson, Jr. *Secretary*, L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.

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Original Communications

THE VALUE OF VAGINAL SMEARS IN THE DIAGNOSIS OF EARLY MALIGNANCY*†

A Preliminary Report

CHARLOTTE A. JONES, M.D., THEODORE NEUSTAEDTER, M.D., AND
LOCKE L. MACKENZIE, M.D., NEW YORK, N. Y.

*(From the Gynecological-Endocrine Clinic, New York Post-Graduate Medical School
and Hospital, Columbia University, and the Strang Clinics of the Memorial
Hospital and the New York Infirmary)*

ANY procedure that facilitates the early diagnosis of a disease as devastating as carcinoma of the uterus deserves serious consideration and extensive trial. In spite of improved therapeutic methods, clinicians are often handicapped by their inability to discover the neoplasm early enough to insure the maximum effect from the available therapeutic measures. Papanicolaou¹⁻³ and his associates, who have studied the cellular details of vaginal smears for a number of years, have opened a field that may eventually revolutionize the story of pelvic carcinoma in women. The material included in this survey is submitted as a preliminary report of the results obtained from the microscopic examination of the vaginal fluid aspirated as a routine procedure from a selected group of gynecologic patients. Papanicolaou does not claim that this method of diagnosis is the final answer to the problem, but the results obtained would seem to indicate that it is a step in the right direction. He further maintains that, "The vaginal smear should be considered as an accessory or preliminary method of diagnosis, and the actual demonstration of malignant cells in the biopsy specimen should be the basis for decision as to the method of therapy."³ In the management of our cases, we too, have felt that patients whose vaginal

*This study was in part carried out by the generous contributions of Jeremiah Millbank, William Burton Jr., and Elise Strang L'Esperance.

†Presented at a meeting of the Section on Obstetrics and Gynecology of the New York Academy of Medicine, January 25, 1944.

smears were indicative of malignancy should be subjected to further study, and that the tissue sections must be the criterion for final diagnosis.

Method of Examination

The method of obtaining the vaginal smear is simple. The equipment necessary for each aspiration consists of a slightly curved glass pipette to which is attached a small rubber suction bulb; two microscopic slides, each equipped with a paper clip; and a fixative (a mixture of equal parts of 95 per cent ethyl alcohol and ether).

The smear is taken before any examining lubricant is used. The labia are separated and the pipette is introduced high into the vaginal vault, with the bulb compressed. As the pipette is withdrawn, the bulb is then slowly decompressed. The material thus obtained is then sprayed over the surface of the slide and spread evenly. Better cellular differentiation is effected when smears are even and thin. The moist slides are immediately immersed in the fixing solution where they may remain for an indefinite period. The vaginal spreads are stained either by Papanicolaou's method,⁴ or by a modification of it developed at our laboratory at the Post-Graduate Hospital.⁵ Both stains have the specific properties for emphasizing maximum nuclear detail, which is of paramount importance for accurate diagnosis, but the examiner's ability to recognize abnormal cells and interpret their histologic peculiarities requires a thorough knowledge of normal vaginal cytology. The diagnosis of malignancy is made from the vaginal smear just as it is from the tissue section, depending upon the presence of cells which exhibit structural abnormalities. In the smear, aberrant cellular forms are much more striking than in the section. Certain characteristic features are recognized as being common to vaginal smears from both cervical and fundal carcinoma. These are evident to the experienced investigator with low-power microscopic examination, and may be enumerated as follows:

1. Large numbers of leucocytes, chiefly polymorphonuclears, are commonly found. These tend to be clumped as well as scattered, and many are seen engulfed by other cells.

2. Bacteria are numerous.

3. Red blood cells are found in varying numbers even in the early stages. Generally, they will have lost their clear-cut outlines and appear crenated, degenerated or as shadow forms. The finding of red blood cells is considered so important, that in their absence, one should hesitate to render a positive diagnosis of malignancy. There are, however, exceptional instances of some very early cases in which red blood cells are not found.

4. The degree of cornification is frequently higher than in smears from nonmalignant cases, and it is common to find the cancer cells themselves cornified.

5. Histiocytes, appearing as single cells, are very common. They are large, foamy, often multinucleated cells, whose cytoplasm engulfs leucocytes, cellular debris and degenerated red blood cells.

6. Bizarre cellular forms are found of varied size and shape. The cytoplasm is hyperchromatic and contains deeply staining granules. Vacuoles are frequently found, and these often contain ingested cellular debris. The nuclei of these cells are dense, granular, irregular in form and may show prophases or arrested phases of mitosis. These are the malignant cells which determine the final diagnosis.

Clinical Investigation

This study includes the examination of 434 patients. Of this number, seven failed to return for proper follow-up; the conclusions, therefore, are based upon 427 cases. Two hundred and forty-five individuals were seen in the Strang Clinic, and one hundred and eighty-two in the Gynecological-Endocrine Clinic of the New York Post-Graduate Hospital. In 91 cases, a diagnosis of malignancy was made from the vaginal smears, of which 82 were confirmed by biopsy or curettage. The diagnosis of carcinoma of the cervix was made in 53 instances; carcinoma of the fundus in 37, and sarcoma of the cervix in 1 case. Of the slides examined at the Post-Graduate Hospital, 43 positive slide diagnoses of cancer were made; 31 of which were of carcinoma of the cervix; 12 cases of carcinoma of the fundus, and 1 of sarcoma of the cervix. Forty-eight positive smears were obtained from the Strang Clinic; 22 of which were indicative of cervical carcinoma, and 25 of carcinoma of the fundus. Confirmation of the vaginal smear diagnosis was obtained through tissue study in all but 9 instances. In 7 cases, a negative smear diagnosis was reported, which was subsequently proved incorrect when curettings were submitted.

The characteristic feature of a smear indicative of carcinoma of the cervix is the aberrant cell which may assume one of many forms. These cells present all the characteristics of a malignant cell and vary in outline. Variations include amoeboid, tadpole, saddlebag and other irregularly shaped cells. The presence of cells such as these, plus the diagnostic features already mentioned, indicates cervical malignancy.

CASE 1.—Mrs. M. H., aged 58 years, was first seen in the Strang Clinic November 25, 1941, complaining of vaginal spotting of 4 months' duration and low abdominal pain. Her past history was irrelevant, and the menopause had occurred at 43 years. At her first clinic visit, vaginal smears and a cervical biopsy were taken.

Vaginal Smear Report: 11/25/41. (Fig. 1.) A large number of polymorphonuclear leucocytes is present and a moderate number of red blood cells. There are many deep cells characteristic of the menopause. In addition, there are numerous plaques of aberrant cells. These are irregular in shape and consist chiefly of tadpole forms. The cytoplasm is hyperchromatic and granular, and the nuclei are dense and contain abnormal granules of various sizes. The smear is consistent with squamous carcinoma of the cervix.

Pathological Report: 11/26/41. (Fig. 2.) A small piece of tissue is present, which is made up almost entirely of large, irregular squamous cells with deep staining nuclei, many of which contain mitotic figures. The stroma is markedly infiltrated with small lymphocytes and some polymorphonuclear leucocytes. The tumor cells are seen to be invading the stroma in several areas.

Diagnosis: Squamous carcinoma of the cervix—Grade II.

Management: The patient was referred to the x-ray department for therapy. Beginning November 26, 1941, she received a cycle of deep x-ray amounting to 2,450 r. to 4 pelvic portals. February 4, 1942, a radon bomb of 1,000 mc. hr. was applied. During this period of treat-

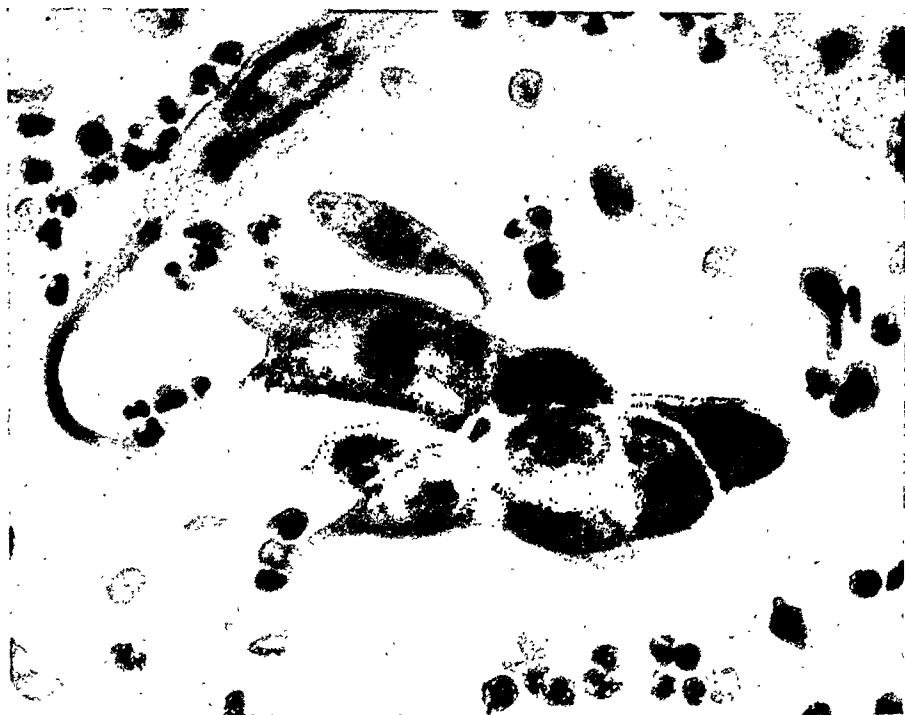


Fig. 1.—Carcinoma of cervix—vaginal smear. Magnification ($\times 810$).

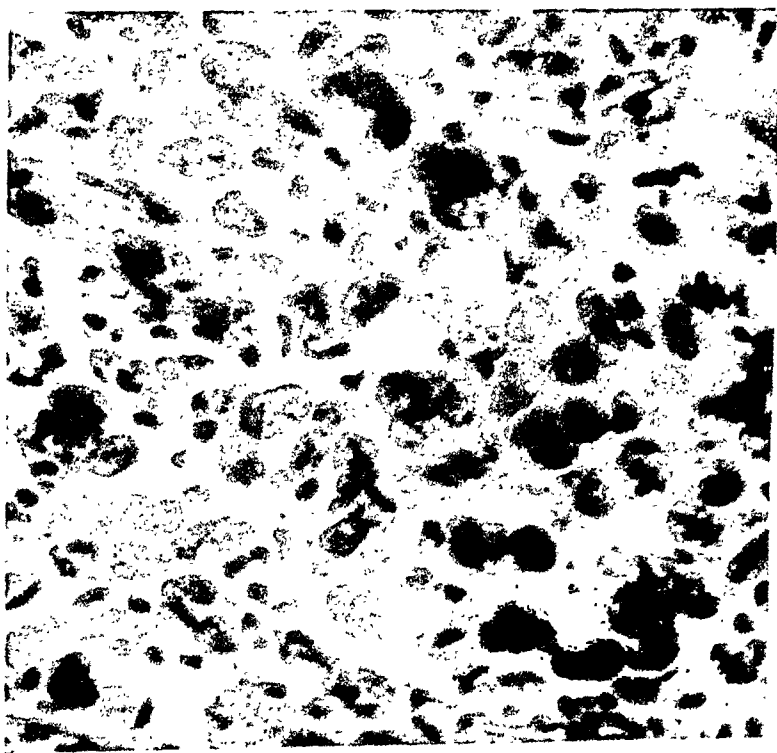


Fig. 2.—High power tissue—carcinoma of cervix. Magnification ($\times 810$).

ment, vaginal smears and cervical biopsies were taken. The first negative smear was obtained in October, 1942. Repeated vaginal smears taken in the follow-up clinic since then have all been negative. Her last clinic visit was December 14, 1942.

The diagnosis of carcinoma of the fundus is based upon the presence of malignant endometrial cells. There were 35 cases in which this diagnosis was made and confirmed. The cell upon which the diagnosis is based is small, round or cuboidal, slightly larger than a leucocyte. The nucleus is large in proportion to the size of the cell, stains deeply and is granular. Vacuoles are a common finding and may be so large and prominent as to displace the nucleus to the periphery, causing the cell to assume a signet-ring appearance.

CASE 2.—Mrs. M. S., aged 56 years, was first seen in the Strang Clinic April 25, 1942, complaining of vaginal bleeding of six weeks' duration. Her menopause had occurred at the age of 47, and was uneventful. Her past history was not significant. She was admitted to the hospital with the diagnosis of uterine fibromyoma April 26, 1942. The following day, a total hysterectomy was performed for degenerating submucous fibroid.

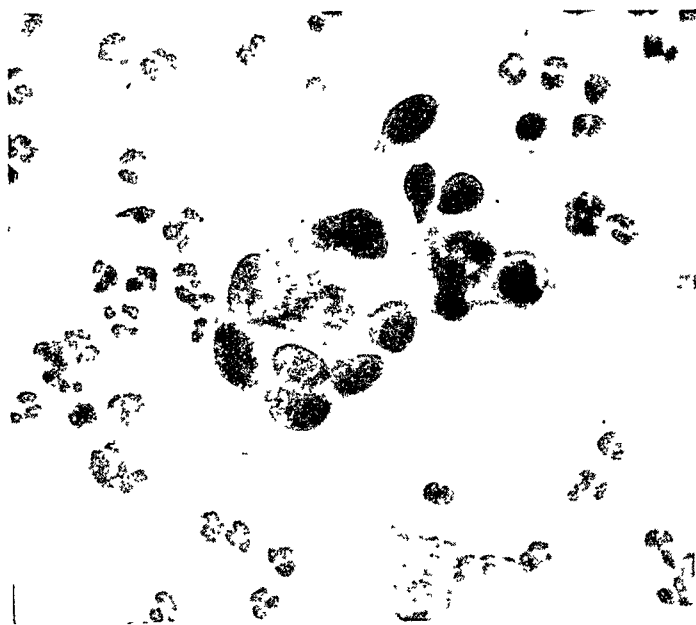


Fig. 3.—Adenocarcinoma of fundus—vaginal smear. Magnification ($\times 810$).

Vaginal Smear Report: 4/25/42. (Fig. 3.) A large number of polymorphonuclear leucocytes is present in addition to a large number of red blood cells. The slide is deep menopausal in type, and malignant cells are seen. These cells consist of clumps of small round cells with large, dense, irregular nuclei. Many are vacuolated and are of the signet-ring type. There are a few amoeboid and tadpole forms. The smear is consistent with adenocarcinoma of the fundus.

Pathological Report: 4/27/42. (Fig. 4.) The uterus measures 11.5 cm. in diameter, and when opened is seen to contain a large extensively degenerated submucous fibroid. On microscopic examination, bundles of smooth muscle cells are seen in the characteristic whorl pattern of the fibromyoma. These interlacing fibers are uniform in size and are intermingled with areas of hyaline tissue. Toward the endometrial surface, there is a moderate amount of necrotic tissue infiltrated with leuco-

cytes and red blood cells. Over the surface of the fibroid and invading it to a moderate degree, are areas of lawless glandular proliferation. The glands are increased in number, and their epithelium is definitely stratified. Numerous mitotic figures are present in markedly hyperchromatic nuclei.

Diagnosis: Degenerating submucous fibromyoma and adenocarcinoma.

Management: Following her discharge from the hospital, the patient was referred to the x-ray department for deep therapy. She received a cycle of deep therapy which was begun May 18, 1942, and completed June 11, 1942, amounting to 2,000 r. to 4 pelvic portals. Vaginal smears have been taken at each follow-up visit. They have all been negative. The patient was last seen in the Strang Clinic January 4, 1943, at which time she was in excellent condition.

The spindle cell is occasionally found in a smear indicative of carcinoma, but when present in these cases, it is not solitary but appears with other more characteristic carcinoma cell forms. When spindle cells are found in the vaginal smear exclusive of all other abnormal cells, it may be considered diagnostic of sarcoma. One such case is included in this study.

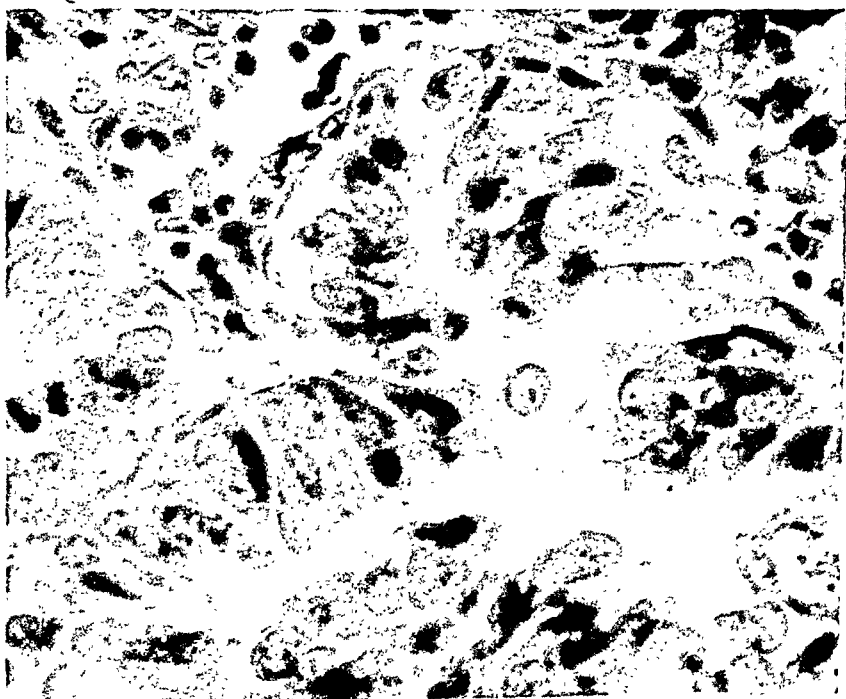


Fig. 4.—Tissue—adenocarcinoma—fundus. Magnification ($\times 810$).

CASE 3.—Mrs. H. K., aged 49 years, was first seen in the gynecological clinic of the New York Post-Graduate Hospital January 13, 1942. At this time, she complained of a bloody vaginal discharge first noticed six months previously, and hot flashes. Her menopause had occurred five years before, when a supracervical hysterectomy for uterine fibroids had been performed at another hospital. On her first clinic visit, vaginal smears and a cervical biopsy were taken.

Vaginal Smear Report: 1/13/42. (Fig. 5.) Enormous quantities of pus are seen. Many of these cells appear in thick clumps. Many deep cells indicating menopause are present. There is a moderate number of hyperchromatic cells with fragmented nuclei, and an occa-

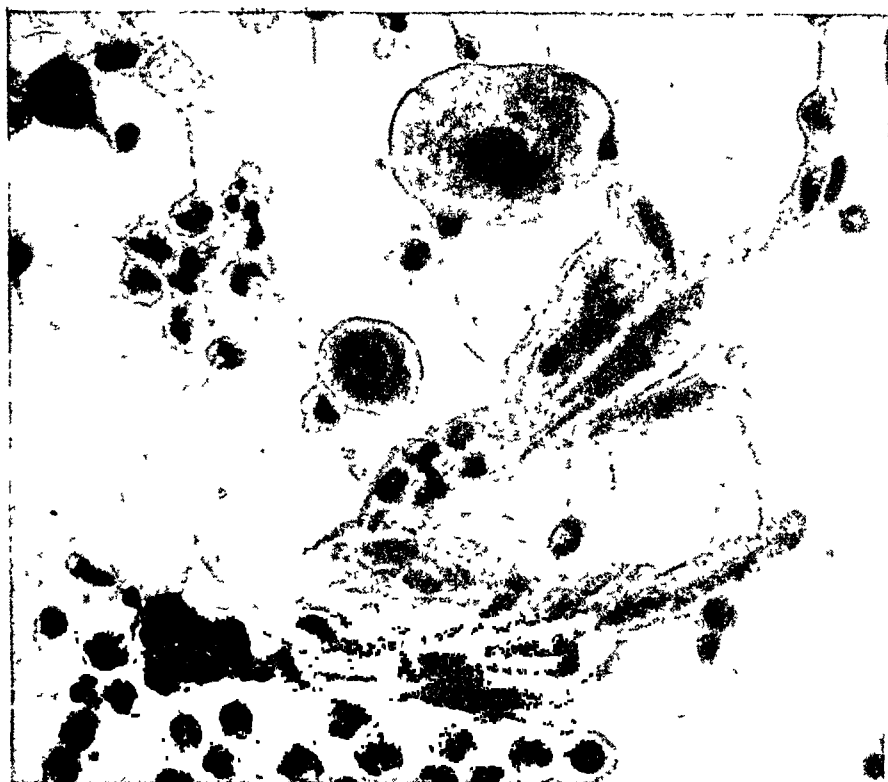


Fig. 5.—Vaginal smear—sarcoma of cervix. Magnification ($\times 810$).

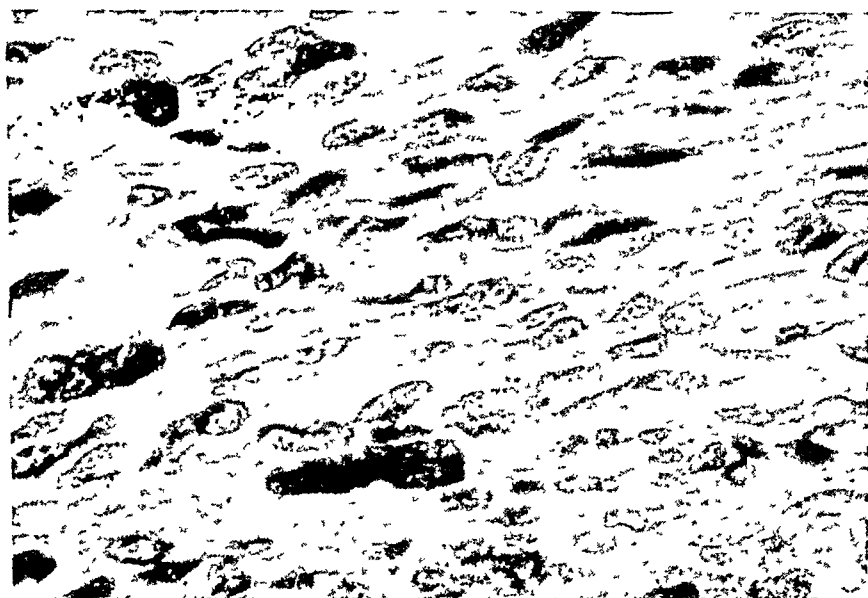


Fig. 6.—Tissue—sarcoma of cervix. Magnification ($\times 810$).

sional group of long spindle cells which do not appear malignant. The interpretation of these is obscure. Diagnosis deferred but suggestive of sarcoma.

Pathological Report: 1/13/42. (Fig. 6.) The tissue is a neoplasm consisting of interlacing bundles of smooth muscle through which courses an intricate network of a few coarse and many fine fibers of collagen and reticulum. The smooth muscle cells show many atypical features. Their nuclei vary abundantly in size, are generally large, oval or cylindrical with rounded ends. They show varying degrees of hyperchromatism. A few giant and bizarre forms are noted. An occasional mitosis is seen. A few foci of sclerosis are present with neoplastic cells isolated in thick fibers of collagen.

Diagnosis: Leiomyosarcoma of the cervix.

Management: The patient was admitted to the New York Post-Graduate Hospital and on January 14, 1942, the cervical tumor stump was excised and radium amounting to 2,080 mc. hr. was applied in six 5 mg. needles. The case has been followed since hospital discharge. Vaginal smears have been negative. She was last seen in the clinic April 13, 1943, at which time the cervix was soft, healed and free from disease.

Discussion

In this study no attempt has been made to designate through the vaginal smear undifferentiated and highly differentiated epidermoid carcinoma. All types of squamous carcinoma of the cervix produce the bizarre cell forms which are characteristic, and when these are found together with other general characteristics of malignancy, the diagnosis of squamous carcinoma is in order. Despite the fact that these aberrant forms are spectacular, it must be remembered that they constitute a relatively small proportion of the total cell elements found, and their discovery frequently requires prolonged search.

The discovery of malignant endometrial cells is attended with great difficulty. This is due to the fact that these small cells are found intermingled with dense masses of red blood cells and leucocytes. In advanced cases where the characteristic malignant fundal cell appears in large plaques, the diagnosis is somewhat simpler. The entire vaginal smear picture of endometrial neoplasm is much less impressive than that of the picture in cervical carcinoma.

Greater variations in size and shape are found in both types of cases where the lesion is advanced, but in addition to the diagnostic cell, there is ordinarily such a heavy content of blood cells and mucus that few cellular elements of any kind are distinguishable.

The apparent high incidence of malignancy in the group of patients examined is explained by the fact that of the total number of cases, approximately 57 per cent were observed at the Strang Clinics, which are exclusively confined to the study of new growths. The remaining patients were registered for endocrine disturbances at the Gynecological-Endocrine Clinic. An additional few were private patients, in whom objective symptoms suggested the possibility of malignancy. The fact that there were three instances of very early neoplasms discovered dur-

ing routine examinations of endocrine patients is of paramount importance, for it definitely illustrates the advantages of routine vaginal smears. The earlier malignant disease is brought to our attention, the sooner proper treatment can be instituted. Consequently, the ultimate number of 5- to 7-year curves should be greatly increased over the 26 per cent which prevails at present.

TABLE I. SUMMARY OF CASES

Total number cases examined		434
Total number cases followed		427
N. Y. Post-Graduate Hospital Clinic	182	
Strang Clinic	245	
Diagnosis of malignancy made from vaginal smear and		
Confirmed by biopsy		
Total cases		82
Strang Clinic	43	
N. Y. Post-Graduate Hospital Clinic	39	
Squamous carcinoma of cervix		48
N. Y. Post-Graduate Hospital Clinic	28	
Strang Clinic	20	
Sarcoma of cervix		1
Carcinoma of fundus		33
Strang Clinic	22	
N. Y. Post-Graduate Hospital	11	
False positive diagnoses		9
Cervix	5	
Strang Clinic	2	
N. Y. Post-Graduate	3	
Fundus	4	
Strang Clinic	3	
N. Y. Post-Graduate	1	
False negative diagnoses (all fundus)		7
Strang Clinic	5	
N. Y. Post-Graduate	2	
Cases referred without clinical diagnosis		129
N. Y. Post-Graduate Hospital Clinic	56	
Strang Clinic	93	
Cases referred with nonmalignant diagnoses		251
N. Y. Post-Graduate Hospital Clinic	190	
Strang Clinic	61	
Cases referred with diagnosis of malignancy		47
N. Y. Post-Graduate Hospital Clinic	7	
Strang Clinic	40	
Total Cases		427

Summary

1. A diagnostic aid in the discovery of early pelvic malignancy has been described and the results of the method as used in 427 cases have been presented.

2. The microscopic characteristics of malignant smears have been outlined and the specific cells designating squamous carcinoma of the cervix, adenocarcinoma of the fundus and 1 case of sarcoma have been described, together with an illustrative case history for each.

3. The importance of confining the method to the realm of preliminary and corroborative procedures is stressed.

Conclusion

From the material presented, we feel justified in concluding that this procedure is worthy of continued trial. Although no claim is made for the infallibility of the test, we feel that even in its present stage of development, it represents a valuable addition to the methods now utilized for the early diagnosis of pelvic carcinoma in women. Furthermore, when suspicious cells are present, even though few in number, the patient should be further investigated. Although most are eventually proved negative, an occasional early lesion will be detected, which otherwise might have been completely overlooked.

References

1. Papanicolaou, G. N., and Shorr, E.: *AM. J. OBST. & GYNEC.* 31: 806, 1936.
2. Papanicolaou, G. N.: *Am. J. Anat.* 52: (suppl.) 519, 1933.
3. Papanicolaou, G. N., and Traut, F.: "Diagnosis of Uterine Cancer by the Vaginal Smear," New York, 1943, Commonwealth Fund.
4. Papanicolaou, G. N.: *Science* 95: 438, 1942.
5. Fuller, Dorothea: *J. Lab. & Clin. Med.* 28: 1474, 1943.

CERVICAL PREGNANCY

A Partial Review of the Literature and a Report of Two Probable Cases*

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CERVICAL pregnancy, admittedly of rare occurrence, has been given but scant consideration in American medical literature. Consulting three of our most widely used textbooks of obstetrics, it is found that two^{1, 2} do not mention the condition, while the third,³ denies its existence. Only one report⁴ can be found since 1900 in the journals of this country.

Notwithstanding this, personal experience and a review of the literature, mainly foreign, offers convincing evidence that this type of gestation actually occurs and often presents serious complications, not infrequently terminating fatally. This unusual variety of pregnancy results from the nidation and development of the fertilized ovum in the structure of the cervix, the corpus uteri remaining uninvolved. It is to be sharply differentiated from the isthmico-cervical pregnancy described by Aufeld and Aschoff.⁵ In the latter cases one finds a placenta previa with an extension into the cervix, the ovum developing in the corpus uteri. Before considering this subject any further, it might be well to outline the events which transpire in the first seven or eight days of the existence of the fertilized human ovum.

It is generally accepted, in a woman with a twenty-eight day menstrual cycle, that ovulation usually takes place between eleven and fifteen days following the onset of the preceding menstruation. It has been established by direct observation that the ovum is slowly extruded onto the surface of the ovary from the ruptured follicle, the explosive action, which one would associate with this process, being lacking.⁶ The ovum is engulfed almost immediately by the fimbriated end of the tube which has been shown to assume unusual activity at this time, sweeping back and forth over both surfaces of the ovary.⁷ After its entrance into the ampulla, where it is believed that fertilization most commonly takes place, the passive ovum is transported by the ciliary current and the coordinated segmental muscular movements of the tube to the uterine cavity. Its course is rapid at first, more slow as it reaches the isthmus, the total time of transportation being approximately ninety-six hours.⁸ After the arrival of the ovum in the

*Presented at a meeting of the New York Obstetrical Society, Nov. 14, 1944.

uterus, it tends to lie in one of the surface crevices of the progestational endometrium in the upper part of the uterine cavity. It is a completely passive object and, while it has changed from a unicellular to a multicellular structure, its total bulk is no greater than when it first emerged from the ovary. It is still enclosed in the zone pellucida. The uterus at this stage of the progestational phase is atonic so that it is not surprising to find, in the two or three days that remain before nidation, that the ovum usually does not move far from the uterine opening of the tube. The development of the human ovum up to this point has not been observed but is believed to follow closely that noted in the rhesus monkey.⁹ At the end of this time, the zone pellucida disappears and the ovum, having reached the point of development termed the blastodermic vesicle, begins to enter the progestational endometrium by a process of digestion and erosion of this structure.¹⁰ Whether it embeds on the anterior or posterior surface of the mucous membrane probably depends upon which of these surfaces is in closest relationship to the embryonic pole of the ovum, which always presents as a spearhead of invasion.

It is impossible to believe that the intrauterine position of this minute structure, the fertilized ovum, can be influenced by gravity, sandwiched as it is between two layers of a succulent progestational endometrium which lines the extremely atonic uterus. Nevertheless, one of our most used textbooks¹¹ seriously discusses the effect of gravity on the position of the unembedded ovum as if it were a die in a dice box.

The fact that the ovum usually travels only a short distance after its delivery by the tube into the uterine cavity is borne out by the position of the placenta at term in the vast majority of pregnant women. It is found usually in the upper corpus attached to the anterior or posterior wall. While this is the common site of the term placenta, it may be found to be attached at lower levels in the uterine cavity. When it is attached so that it encroaches on or covers the internal os, we term the abnormal attachment placenta previa.

It is probable that many placenta previas are formed secondarily, through a persistence of a part of the chorion laeve by the process described by Hoffmeyer. In some instances, however, they result from primary nidation low in the uterine cavity close to the internal os. Occasionally such an implantation may show an extension of the placenta into the cervical canal. As an example, witness the microphotograph made from a section of curettings obtained from a patient with a two months' inevitable abortion at Bellevue Hospital a few years ago (Fig. 1). It shows chorionic villi embedded deeply into mucosa characteristic of the upper cervix. In short, the behavior of the Müllerian tract during the early days of pregnancy is such that nidation of the ovum in the most favorable upper part of the uterine cavity is almost certain. Only occasionally does this complex mechanism fail.

There remains, however, one more possibility. Suppose that the fertilized ovum, making a rapid transit of the uterine cavity under the influence of factors, unknown but probably largely accidental, enters the cervical canal before it is capable of nidation and embeds itself in the surface mucosa of this structure before reaching the external os. There is no evidence to show that the cervical mucosa possesses a special power to resist the erosive and destructive effect of the trophoblast. Neither does it possess the function of the progestational endometrium, and later the decidua, of limiting this invasive and destructive action to the superficial cellular layers of the mucous membrane. There is no reason to doubt that such an ovum can penetrate to varying depths in the cervical wall, can create a blood space by opening maternal vessels, and continue its development for a certain length of time.



Fig. 1.—Bellevue Hospital Accession No. 3595/35. Curettings from early abortion showing chorionic villus implanted in mucosa, whose stroma and glands resemble these of the isthmus or upper cervix.

Referring to the literature, a very interesting group of cases, almost entirely confined to the European journals, is found to support this theoretical possibility. These cases can be divided into two groups, in the first of which the presence of a cervical pregnancy is backed by pathologic evidence, in the second of which such a gestation is to be suspected on clinical evidence, more or less well defined.

TABLE I. CASES OF CERVICAL PREGNANCY PROVED BY PATHOLOGICAL EXAMINATION OF UTERUS (OPERATIVE SPECIMENS OR AUTOPSY)

AUTHOR, YEAR OF REPORT	AGE, PARITY	DURATION OF PREG- NANCY	BLEED- ING IN EARLY WEEKS	EN- LARGED CERVIX	CORPUS NOTED ABOVE CERVIX	PREOP- ERATIVE DIAG- NOSIS	TREATMENT	TRANS- FUSION	RESULT	PATHOLOGY
1. Tarnier, 1887 ¹²	39 P.O. G.1	Term 40 wk.	?	Cervical fibroid present- ing at exter. os.	0	Labor ob- structed by fibroid	Cesarean section	0	Died 2 hr. P.O.	Autopsy: Small corpus above distended thin cervix con- taining fibroid and pla- cental site
2. Franz, 1899 ¹³	41 ?	6 to 8 wk.	+	+	+	Cancer of cervix	Total hysterectomy	0	Recovery	Path.: Placenta implanted in cervix
3. Pankow, 1910 ¹⁴	46 P.9	20 wk.	+	Enlarged and ex- panded	+	Late abortion	1. Manual removal of placenta 2. Tamponade (twice) 3. Total hysterectomy	0	Recovery	Path.: Placenta inserted in anterior wall of expanded cervix. No decidua in corpus
4. Jaschke, 1910 ¹⁵	39 P.7	12 wk.	+	Enlarged cervix	Corpus re- troverted	Abortion	1. Tamponade 2. Vaginal hysterot- omy 3. Total vaginal hysterectomy	0	Recovery	Path.: Placenta inserted in anterior wall of cervix. Slight decidual reaction in corpus
5. Goodman, Rubin, 1911 ¹⁶	28 P.2 G.5	16 wk.	0	+	0	Ruptured ectopic	Supravaginal hyster- ectomy. Removal of placenta from cavity in cervix	0	Recovery	Path.: Placenta implanted in right side of cervix. Decidua in corpus
6. Tiegel, 1915 ¹⁶	36 P.3 G.6	12 wk.	+	+	+	Abortion	1. Packing 2. Curettage of cervix 3. Total hysterectomy	0	Died Sepsis	Path.: Placenta implanted in cervix. Decidua in corpus

7. Reinhardt, 1924 ¹⁷	24 P.0 G.1	8 wk.	0	+	+	+	Abortion	1. Curettage 2. Tamponade 3. Total hysterectomy	0	Recovery	Path.: Placenta implanted in right side of cervix. No decidua in corpus
8. Bacalli, 1926 ¹⁸	36 ♀	12 wk.	+	+	0	0	Abortion	1. Curettage 2. Tamponade 3. Total hysterectomy	0	Died 4 days anemia	Path.: Placenta implanted in cervix. No decidua
9. Gans- bauer 1927 ¹⁹	32 P.1 G.2	22 wk.	0	+	Noted at operation	Placenta previa	Total hysterectomy	Total hysterectomy	0	Recovery	Path.: Placenta implanted in cervix. Decidua scanty in corpus. Diverticulum of membranes in corpus
10. Meyer, 1929 ²⁰	27 P.0 G.1	12 wk.	0	+	(Thought to be fibroid)	Early preg- nancy	1. Cervical hysterot- omy 2. Total hysterectomy	1. Cervical hysterot- omy 2. Total hysterectomy	0	Recovery	Path.: Placenta implanted in posterior cervix. Decidua in uterus
11. Kleiner, 1929 ²¹	23 P.1 G.3	10 wk.	+	+	Mainly right side	Incom- plete abortion	1. D. & C. 2. Tamponade 3. Total hysterectomy	1. D. & C. 2. Tamponade 3. Total hysterectomy	0	Recovery	Path.: Placenta implanted in cervix on right
12. Cousse, 1931 ²²	37 P.7 G.8	16 wk.	+	+	+	Late abortion	D. & C.	D. & C.	0	Died	Path.: Placenta implanted in cervix. (Post-mortem hysterectomy)
13. Schürger, 1937 ²³	32 P.2 G.3	10 wk.	+	+	+	Hema- toma of cervix	1. D. & C. 2. Resection of cervix	1. D. & C. 2. Resection of cervix	0	Recovery	Path.: Placenta implanted in cervix
14. Desirotte, 1940 ²⁴	38 P.0 G.1	12 wk.	+	+	+	Cervical fibroid	Total hysterectomy	Total hysterectomy	0	Recovery	Path.: Placenta implanted in cervix

The first group of cases, numbering fourteen, has been summarized in Table I. In all of these cases, except two,^{4, 23} the relationship of the placenta solely to the cervix was established beyond doubt by pathologic examination of the entire uterus, obtained by operation or on post-mortem examination.

A consideration of these proved cases of cervical gestation discloses that the patients varied in age from twenty-three to forty-six, ten of the fourteen women being over thirty, and eight out of the ten being over thirty-five. Eight of them were multiparas; four were primiparas, while in two instances the parity of the patient was not stated. In only one of the multiparas was there a history of a previous obstetrical complication; this patient¹⁹ carried her previous pregnancy to term, the fetus being delivered by a destructive operation through an incompletely dilated cervix. There is nothing in the history of these patients, except a tendency to belong to an older age group, to suggest an etiological factor other than an accidental one.

As one would expect from the unfavorable nidation site, the ovum rarely develops to term, Tarnier's¹ case being the only exception. In ten of the fourteen cases the pregnancy was terminated at or before the sixteenth week because of the chief complication, hemorrhage. In Meyer's²⁰ patient the character of the pregnancy was accidentally discovered during the course of a therapeutic abortion performed at the twelfth week. The longest that the two^{14, 19} remaining patients carried their pregnancies was twenty-two weeks.

The commonest symptom in the early weeks was vaginal bleeding in varying amounts. The onset was sometimes so early that no history of amenorrhea was obtained, obscuring the diagnosis of pregnancy. Early bleeding was absent in four cases,^{4, 17, 19, 20} being present in nine, while in one patient¹² this detail of the history was ignored. When present, the bleeding tended to become more profuse as the pregnancy grew older, eventually compelling medical intervention. The other symptoms noted were principally vague lower abdominal discomfort and backache, and occasional disturbances of urination.

Examination of these patients showed the systemic evidence of hemorrhage if bleeding had been profuse. In the patient whose pregnancy had proceeded beyond the third month, abdominal examination revealed a mass, rising from the pelvis, corresponding in size to the duration of the pregnancy. Above this mass and attached to it was sometimes noted the firmer, smaller uterine corpus, which usually was mistaken for a uterine fibroid. Except in the case reported independently by Goodman and Rubin, in whom the main signs detected were those of intraperitoneal hemorrhage, no other abdominal signs were present.

On bimanual examination obvious uterine bleeding was present. The striking finding was enlargement and expansion of the cervix which, naturally, progressively increased in size with the duration of the

pregnancy. Its consistency usually misled the examiner into believing that it was the pregnant corpus. When such pregnancies proceeded beyond the twelfth week, the external os was often found to be partly dilated, enabling the examiner to feel the sac, just above the opening, and sometimes the lower edge of the placenta.¹⁹ In nine instances the small, firm corpus could be made out above the cervical mass. On one occasion this peculiarity could not be observed because of retroversion of the uterus.¹⁵ Except for the absence of a history of preceding painful expulsive uterine contractions the findings were often similar to those noted in the cervical stage of the abortion of a normally implanted ovum.

The diagnosis entertained in most instances was that of early or late uterine abortion. Early placenta previa was considered in one patient, while in another, who had exhibited no bleeding, normal uterine pregnancy complicated by fibromyomata was thought to exist. In the early cases with bleeding from the onset and no amenorrhea, the presence of a cervical neoplasm was suspected on two occasions.^{13, 24} In one patient, because of the signs of intraperitoneal hemorrhage, the diagnosis of ruptured tubal pregnancy was made.⁴

In eight of the patients attempts were made to evacuate the products of gestation by the vaginal route. When closed, the external os was dilated, and once vaginal hysterotomy was employed.¹⁵ Removal of the placenta proved difficult and usually could only be accomplished in piecemeal fashion. Profuse violent hemorrhage immediately occurred which proved difficult or impossible to control with tamponade. This necessitated the performance of total abdominal or vaginal hysterectomy in six patients,^{14-18, 21} while in one, the bleeding was controlled by cervical amputation.²³ The eighth patient died almost immediately of hemorrhage and shock.²² Of the six remaining patients four were treated with total hysterectomy,^{13, 19-20, 24} usually carried out under mistaken diagnosis, one was delivered by Cesarean section performed through the thin, expanded cervix,¹² while one was treated by supravaginal hysterectomy;⁴ the hemorrhage from the cervical stump being controlled by mass ligation of tissue. It is striking to note that not once was transfusion utilized in this group of individuals, most of whom suffered from acute and massive blood loss.

Four^{12, 16, 18, 22} of the fourteen patients failed to survive, a mortality of almost 30 per cent. The cause of death was hemorrhage and shock principally, but in one instance,¹⁶ severe infection played an additional part in the death of the patient.

The pathologic findings are of considerable interest. Tarnier's¹ case showed at autopsy a greatly distended, thin-walled cervix containing a large cervical fibroid and the placental site. It was surmounted by a firm contracted corpus uteri, quite uninvolved in the pregnancy. The only chance of saving this patient would probably have been the per-

formance of a complete hysterectomy after the removal of the fetus by Cesarean section. Goodman and Rubin's⁴ case is of interest mainly from the viewpoint that the corpus shows a well-developed decidua but no evidence of chorionic invasion. The first evidence of chorion was encountered in the upper cervix which was removed with the body of the uterus.

Schürger's²³ specimen, obtained by amputation of the cervix, shows the nidation site deep in the cervical wall and apparently about to rupture into the lateral vaginal fornix. At operation the cervix was noted to be asymmetrically enlarged and deep blue in color.

In the remaining specimens the whole uterus was available for examination. In all of them the placental implantation appeared to be confined to the cervix. However, owing to the fact that preliminary operative procedures had been utilized at varying intervals before the removal of the uterus in all but one patient,¹⁹ in only the latter instance was the specimen intact. A decidual lining of the corpus could not always be demonstrated especially when the hysterectomy was performed some time after preliminary curettage, but was generally noted when the uterus was promptly removed.^{4, 15, 16, 19, 20}

Examination of the cervix showed no evidence of cervical glands beneath the placental site, the chorionic villi penetrating and being directly attached to the cervical muscularis. The cervical muscularis was very thin, particularly in the more advanced pregnancies but was usually not deeply invaded, the ovum expanding in the direction of the cervical canal. However, in Rubin's case perforation of the supravaginal cervical wall occurred into the base of the broad ligament; while in Schürger's²³ case, such a perforation had almost taken place into the lateral vaginal fornix. Abundant large vessels, both arterial and venous, were present in the cervical wall. These findings readily explain the difficulty in removal of the placenta and the violent hemorrhage which follows such efforts.

Here can be mentioned a case, reported by Connors et al.,²⁵ which was not included in Table I because of its remarkable character. A forty-four-year-old woman, who had undergone a supravaginal hysterectomy three years previously and who had subsequently showed amenorrhea, was admitted to a hospital for lower abdominal pain and a yellowish discharge. On examination the cervix was found to be effaced, the external os being dilated to 4 to 5 cm. A fetal head presented. The fetus was delivered and survived for over thirty hours, weighing 896 grams. The placenta did not separate. On attempting to remove it, it was found to be densely adherent to a thin-walled cavity. It was removed piecemeal and incompletely, accompanied by profuse hemorrhage which was controlled by packing. Because of continued bleeding the abdomen was opened. A large thin-walled sac, centered in the pelvis, was found which was continuous with the cervix and to which both tubes and ovaries were attached. This was removed. Pathologic examination showed the wall to be made up of

smooth muscle. No glands were identified. Connors interpreted this case as a left tubal pregnancy which developed to the sixth month. He thought that tubal contractions had brought about the dilatation of the cervix. In the light of the cases just reviewed it would seem more likely that this represents an instance of cervical gestation, following supravaginal hysterectomy, and the development of continuity between the lumen of a tube and the cervical canal.

The second group, also fourteen in number, has been summarized in Table II. These patients all escaped radical operation, the pregnancy having been evacuated by the vaginal route, with successful results except in two instances, in spite of the fact that transfusion was only used in one patient.³⁴ The details of these cases conform in the main with the features which already have been emphasized in the discussion of the data in Table I. Of course, one must depend on the clinical observations of those who reported the cases and certainly, in some instances, the evidence is not too strong. Wolters'²⁶ second case, a fatality, is so scanty in detail that one must discard it from consideration. Case 1 of Tropea,²⁸ Case 2 of Bolaffi,²⁹ and the case reported by Hyslop³⁰ suggest strongly that the condition encountered was the cervical stage of an ordinary uterine abortion, because of the absence of evidence of any strong attachment of the placenta to the cervical wall and because the removal of the ovum was not followed by violent hemorrhage. In two of the above cases the description of the ova suggests advanced degeneration. The remainder strongly suggest that the pregnancy was fully implanted in the cervical canal.

Excluding the four cases mentioned above, the maternal mortality amounts to about 10 per cent. Combining both groups of cases the mortality is found to be a little more than 20 per cent.

The cases summarized in these tables do not pretend to represent a full review of the literature and, undoubtedly, other reports on this condition have escaped notice. It is believed that many such cases escape diagnosis, or if recognized, are not reported in the literature.

Interest in this rare type of pregnancy was stimulated by the observation of two patients in whom all the clinical evidence points to the primary nidation site as being in the cervix. Unfortunately, no pathologic evidence accompanies these records so that they only can be considered presumptive instances of cervical gestation.

Case Reports

Case 1.—Mrs. F. R., aged 40, para i, gravida ii, was first seen on January 23, 1939, complaining of irregular bleeding. Her first pregnancy occurred in 1927 and was normal. She was delivered at term by breech extraction. This child had died at the age of seven from mastoiditis.

Her menses had always been regular, appearing at twenty-eight-day intervals, lasting four days with no pain. The last normal period had occurred December 1, 1938. About December 8, she began to have slight vaginal staining which had recurred at intervals. Her breasts had been swollen and tender and she had suffered from slight nausea.

TABLE II. CASES OF CERVICAL PREGNANCY BASED ON CLINICAL EVIDENCE

AUTHOR. YEAR OF REPORT	AGE, PARITY	DURA- TION OF PREG- NANCY	BLEED- ING IN EARLY WEEKS	EX- LARGED CERVIX	CORPUS NOTED ABOVE CERVIX	PREOP- ERATIVE DIAG- NOSIS	TREATMENT	TRANS- FUSION	RESULT	REMARKS
1. Devreigne, 1911 ¹²	39 P.2 G.6	26 wk. Fetal death at 16 wk.	0	+	+	Late missed abortion	1. Manual and instru- mental removal (incomplete) 2. Tamponade	0	Recovery	Placenta implanted in expanded cervix. Corpus above, empty
2. Wolters, 1921 ²³	26 P.3 G.6	20 wk.	+	+	Noted at operation	Late abortion	1. Manual removal 2. Tamponade	0	Death	Fetus removed through partly di- lated ext. os. Placenta re- moved piecemeal from cervical wall. Corpus above, empty
3. Wolters, 1921 ²³	? ?	12 to 14 wk. Fetus expelled	?	?	?	Late abortion	Placenta removed piecemeal with in- struments	0	Death	Placenta removed piecemeal from distended cervix. Character of corpus not noted
4. Racciatelli, 1927 ¹⁸	25 P.1 G.2	6 wk.	+	+	+	Early abortion	1. Tamponade 2. Curettage and tamponade	0	Recovery	Aborted part of early ovum. Pro- fuse hemorrhage not controlled by packing. Inspection and curettage of cervix; packing. Curettings showed no chorion
5. Racciatelli, 1927 ¹⁸	32 P.0 G.1	8 wk.	0	+	+	Cervical preg- nancy	Cervical hysterotomy	0	Recovery	Cervix incised and ovum removed. Implantation site seen in cer- vical canal
6. Tropea, 1929 ²⁴	29 P.2 G.4	12 wk.	?	+	Retro- verted	Early abortion	Dilatation and curet- tage	0	Recovery	Size and character of ovum sug- gests degeneration. Attachment to cervix not convincing

7. Tropea, 1929 ²⁸	38 P.6 G.15	16 wk.	0	+	+	Late abortion with ruptured mem- branes	1. Tamponade 2. Manual removal	0	Recovery	Placenta adherent to left side of cervical canal. Fundus above, empty
8. Bolaffi, 1932 ²⁹	37 P.1 G.2	6 to 8 wk.	+	+	+	Abortion	Dilatation and curet- tage	0	Recovery	Cavity identified in cervical wall. Corpus above and empty
9. Bolaffi, 1932 ²⁹	39 P.1 G.2	8 wk.	0	+	+	Early abortion	Dilatation and curet- tage	0	Recovery	Ovum protruding from external os. Implantation site identified in cervical canal
10. Hyslop, 1935 ³⁰	35 P.0 G.1	8 to 10 wk.	0	+	+	Early abortion	Dilatation and curet- tage	0	Recovery	Ovum apparently implanted in cervix. Description suggests degenerating early pregnancy
11. Iolkin, 1936 ³¹	35 P.0 G.3	18 to 20 wk.	0	+	+	Late abortion	1. Dilatation of cervix 2. Manual and instru- mental removal of placenta 3. Tamponade	0	Recovery	Placenta implanted in distended cervix. Piecemeal removal. Cavity of corpus identified above
12. D'Aprile, 1937 ³²	32 P.1 G.2	8 wk.	+	+	+	Early abortion	1. Dilatation and curettage 2. Tamponade 3. Tamponade 4. Curettage	0	Recovery	Ovum implanted in canal. Re- moved with difficulty from pos- terior wall. Path.: Villi invad- ing cervical tissue
13. Wittrin, 1938 ³³	29 P.2 G.4	8 wk.	+	+	+	Early abortion	1. Dilatation and curettage 2. Tamponade	0	Recovery	Ovum firmly attached to wall of distended cervix. Corpus iden- tified above, empty
14. Reist, 1941 ³⁴	34 P.3 G.6	23 wk.	0	+	+	Late abortion	1. Manual removal (incomplete) 2. Repeated tamponade 3. Manual removal (14th day) complete	+	Recovery	Rupture of amniotic sac with pas- sage of fetus. Placenta im- planted on posterior left side of distended cervical canal. Corpus above, empty

Examination showed a healthy, well-developed, middle aged female. General examination proved quite normal. Pelvic examination showed a parous introitus and excellent pelvic support. The cervix was posterior, slightly enlarged, soft and normal in appearance. On speculum examination no evidence of bleeding was present. On bimanual examination the corpus was in anterior position, slightly enlarged and soft. The adnexa were negative. No tenderness was present. The findings were suggestive of an early uterine pregnancy. An Aschheim-Zondek test was performed which was reported as positive. She was advised to limit her activity, spending as much time resting as possible.

She was next seen on February 24, and in the meantime noted slight bleeding on several occasions, not accompanied by cramps or pain. Since the corpus uteri could be palpated abdominally just above the symphysis, a vaginal examination was not performed.

On March 11, and again on March 13, she observed slight spotting and shortly after the last occasion passed a quantity of clear fluid per vaginam, without experiencing any other discomfort. Reporting this incident, she was advised to enter the Sloane Hospital immediately (Case No. 574807). On examination after admission, the fundus uteri could barely be felt abdominally. On bimanual examination, the cervix was posterior and gave the impression of being flush with the vaginal vault and fully retracted. The supravaginal cervix was greatly expanded, the uterine mass approximating in size a three and one-half months' pregnancy. The external os was a finger tip dilated with a very thin margin and just above it the fetus could be palpated. No bleeding was taking place, but amniotic fluid was escaping. In spite of the absence of show or painful contractions, these findings suggested a late inevitable abortion, in which the ovum had been forced into the expanded upper cervix. It was expected that the process would be easily completed with the stimulation of contractions by means of pituitrin. However, this anticipated result failed to occur in spite of repeated injections of this agent over the next six days. Slight cramps followed each injection and slight intermittent vaginal bleeding occurred. Examination showed no change in the condition of the cervix. On March 19, she suddenly developed a fever of 103.8° F. accompanied by a shaking chill. Because of this evidence of amniotic sac infection, it was decided to empty the uterus surgically.

Examination under gas oxygen anesthesia revealed the same findings as have previously been described. No bleeding was evident. The thin rim of cervix about the external os was dilated easily, permitting the delivery of a three and one-half months' fetus. The placenta which appeared firmly attached was then grasped with a sponge stick and removed. A sudden, violent and profuse hemorrhage, estimated at well above 1,000 c.c. followed this procedure, and was controlled with difficulty by packing. This incident prevented a more careful investigation of the exact location of the placenta. The patient recovered consciousness rapidly following the termination of anesthesia, but showed a mild degree of shock, her pulse being rapid and soft and the blood pressure was 90/60. She was given a 500 c.c. transfusion and was returned to her room in fair condition. The following day a blood count showed 2,740,000 red cells and a hemoglobin of 56 per cent. The packing was partly removed on March 20, and completely on March 21. She had one more chill accompanied by a rise in temperature to 102° F. A culture from the amniotic sac taken at the time of operation showed *streptococcus viridans*. She was given sulfapyridine, but this was discontinued in a few days.

when her temperature fell to normal. A second transfusion of 500 c.c. was given on March 21, following which her blood count rose to 3,140,000 with 66 per cent hemoglobin. Although slight bleeding continued she was allowed out of bed on March 28, nine days after the evacuation of the uterus. Shortly after this the vaginal bleeding increased, and she began to pass large clots. A rise in pulse and pallor soon appeared. She was returned to the operating room, given a transfusion of 500 c.c. and examined under anesthesia. The cervix was found to be widely dilated, the entire cervical canal being greatly expanded. On the left lateral wall was a mass of adherent placental tissue about four cm. in diameter. At the summit of this space was a constriction through which the examining finger could be passed into the cavity of the corpus uteri, which felt perfectly smooth. The removal of the adherent placental fragments by sponge stick was attended again by sudden, violent and profuse hemorrhage which was controlled by packing. The patient, however, went into deep shock with an almost imperceptible pulse and a blood pressure of 70/16. A second 500 c.c. transfusion was given following which her condition gradually improved so that at the end of eight hours, it was possible to return her to her room.

The packing was partly removed on March 30, and wholly on March 31. Barring moderate fever for a few days and a marked secondary anemia, for which she was given a 750 c.c. transfusion on April 2, her recovery was uneventful. She was discharged twenty-eight days after admission on April 10, 1939, with a red count of 3,400,000 and a hemoglobin of 73 per cent. Normal findings were present on pelvic examination. She has been seen on several occasions since this date and presents nothing noteworthy as regards to either symptoms or physical findings.

In this patient the possibility of cervical pregnancy was not considered until the uterus had been explored the second time. However, there were a number of striking features which were noted before this procedure was carried out and which made no impression on this observer because he had never seen or heard of cervical gestation. Following rupture of the membranes, examination showed the greatly expanded and enlarged cervix of an incomplete abortion. However, there was a complete absence of any of the painful uterine contractions, which must precede such a stage. Moreover, there had been no bleeding other than the slight occasional staining which had been noted ever since the pregnancy had first been suspected. The use of pituitrin on several successive days failed to produce the result which one might confidently expect if the patient had a corporeal abortion. Repeated examinations failed to show any evidence that the presumed uterine abortion was pursuing its expected course.

The fact that the corpus surmounted the cervical mass escaped notice until the final examination under anesthesia but must have been detectable at a much earlier time. Such observations are not in the least characteristic of corporeal abortion and if encountered again by this observer will lead him to suspect a cervical gestation with rupture of the sac into the cervical canal. This case resembles the majority of the instances summarized in Tables I and II.

Case 2.—Mrs. A. G. (Chart No. 206774), was admitted to Bellevue Hospital on January 10, 1942, complaining of profuse vaginal bleeding. Her last menstrual period had occurred in October, 1941. The course of her pregnancy was uneventful until a few hours before her admission, when she developed severe backache and began to bleed profusely from

the vagina. She repeatedly denied any attempt at induction. Her temperature was normal and her pulse 100. Her red blood count was 3,000,000; hemoglobin 64 per cent; sedimentation rate normal; and urinary findings negative.

General physical examination revealed no noteworthy findings. Abdominal examination was negative. Pelvic examination showed a nulliparous introitus and excellent support. The cervix was posterior and one finger dilated. In the right posterolateral aspect of the vaginal cervix was an irregular lacerated area from which protruded a large mass of placental tissue; this was removed. Exploration of this laceration with a finger revealed a cavity in the wall of the cervix which did not pass upward and which was separated from the cervical canal by a thin septum. The uterine corpus was anterior and was moderately enlarged. The adnexa and parametrial areas were normal. At the end of this examination bleeding was only moderate. There is no way of determining the appearance of this cervix before the rupture occurred, but undoubtedly it must have been asymmetrically expanded and enlarged. The patient appeared in mild shock and received a transfusion. Complete hysterectomy was recommended unless bleeding ceased. Unfortunately, for the complete elucidation of this case, bleeding soon stopped and the patient pursued an uneventful afebrile course in the hospital.

Before discharge examination showed the cervix to be firm and closed. The corpus was in anterior position and well involuted. The adnexa and parametrial tissues appeared normal. On the right lateral aspect of the cervix was a healing laceration which bled slightly on manipulation.

Histological examination of the placenta showed it to be made up of fresh, well-preserved villi.

This patient returned to the Hospital on July 12, 1943, when she was delivered of a normal term infant by low forceps. Bilateral lacerations of the cervix of moderate extent were noted and repaired. Otherwise the cervix appeared normal.

As an alternative to classifying this patient as a cervical pregnancy, one might consider her to be an example of a crudely performed induced abortion. The location of the cavity in the cervical wall without communication with either corpus or cervical canal is against this; as well as the normal course pursued by the patient once the abortion was complete. This case is a probable example of the termination of a cervical pregnancy by rupture into the vaginal fornix. This case is very similar to the one reported by Schürger.²³

Comment

It seems probable from the evidence which has been presented that, on rare occasions, the fertilized ovum transverses the uterine cavity before the seventh day of development and, having reached the cervical canal, embeds itself in its mucosa. The depth to which it penetrates is variable as is the level at which it undergoes nidation. Probably complete penetration of the mucosa takes place, since the chorion frondosum develops in relation to the muscularis. It seems likely that many of these pregnancies may terminate in abortion at a very early stage because of the unfavorable site of nidation and so escape recognition. In most instances, when the development continues, the ovum

expands towards the cervical canal carrying before it the mucosa which functions as a decidua capsularis. Very probably early degenerative and necrotic changes occur in the overlying mucosa, which is not functionally adapted to such a process. This may account for much of the early bleeding. With the gradual expansion of the ovum the cervix becomes a thin-walled globular structure, on the summit of which can be felt the corpus, slightly enlarged and firm, and uninvolved in the gestation. In response to the pregnancy the cervix becomes highly

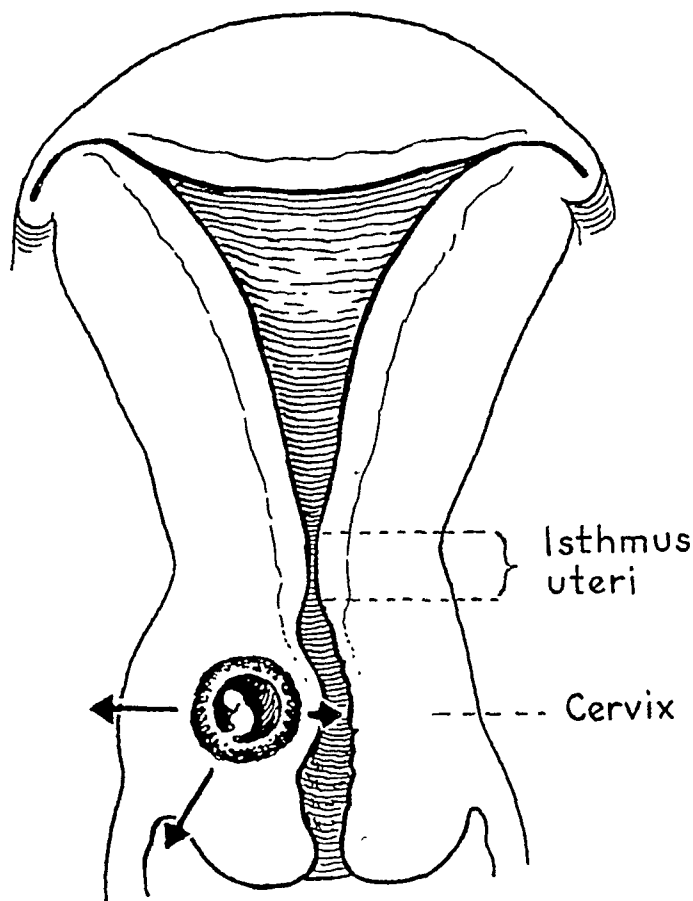


Fig. 2.—Diagram showing four weeks' old ovum implanted in cervix. Further development leads to (1) expansion of cervical mucosa overlying nidation site in character of cervical canal; or (2) rupture of infra- or supravaginal cervix if the cervical muscularis is deeply invaded by chorion.

vascularized; the external os may become dilated. Less commonly, the chorionic invasion may so damage the cervical muscularis by penetration that rupture is imminent or may actually take place. When the lower cervical wall is weakened, rupture can take place into the vault of the vagina. When the upper cervical wall is attenuated, rupture can take place either into the base of the broad ligament, or beneath the bladder, or into the cul-de-sac with the formation of hematomas or intraperitoneal hemorrhage. (Fig. 2.)

Commonly, this type of pregnancy invites surgical intervention before the fourth or fifth month by the occurrence of profuse hemorrhage, by

rupture of the amniotic sac, or by actual perforation of the cervical wall. Unless careful observation reveals the unusual characteristics of a cervical gestation, the diagnosis will usually be missed. On attempting to remove the placenta, it is found to be firmly attached and comes away in fragments and incompletely. Violent hemorrhage, difficult to control with tamponade, accompanies these measures. In the proper management of such cases repeated transfusions, in large quantities, are necessary. With them, the usual case of cervical pregnancy may be evacuated by the vaginal route with a fair degree of safety. When, however, such a pregnancy has proceeded past the fourth month complete hysterectomy may be the safer approach to this problem.

In closing, it is to be emphasized that cervical pregnancies may be regarded as rare and unusual types of ectopic pregnancy. The placental attachment has certain of the features of placenta accreta. The cervix seems only slightly more adaptable than the Fallopian tube to the nidation of the ovum and the continuation of the pregnancy to term. Fortunately, cervical pregnancy is far rarer than tubal gestation, since it is much more difficult to treat from a surgical point of view.

Conclusions

1. Cervical pregnancy is a definite, though rare, entity. Many cases may be unrecognized.

2. Such pregnancies are rarely carried beyond the twentieth week of gestation. Usually it is necessary to intervene surgically before the fifth month because of hemorrhage, rupture of the amniotic sac, or perforation of the cervical wall.

3. Profuse and violent hemorrhage accompanies the attempt to remove the placenta.

4. Enlargement and expansion of the cervix accompanied by bleeding in the early months of pregnancy, the detection of the corpus uteri surmounting the cervical mass should be regarded as suggestive of this condition.

5. Supravaginal rupture of the cervix should be treated by prompt and radical surgery.

6. Intravaginal rupture of the cervix can sometimes be treated more conservatively; however, this complication may require cervical amputation or complete hysterectomy to control hemorrhage.

7. When perforation is not present, in most instances the placenta can be evacuated; partially or completely, either manually or instrumentally; the hemorrhage can be controlled by packing.

8. Blood for transfusion should be available in quantity to combat the large blood loss which may be expected in cases treated by placental removal.

9. With the use of large and repeated transfusion, it is believed that the need for radical operation in the treatment of this condition can be sharply reduced.

10. However, on the rare occasion when such a pregnancy progresses beyond the fourth month, complete hysterectomy may well be the safer approach.

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References

1. Beck: *Obstetrical Practice*, 3 ed., Baltimore, 1942, Williams & Wilkins.
2. De Lee, J., Greenhill, J. P.: *Principles and Practice of Obstetrics*, 8 ed., Philadelphia, 1943, W. B. Saunders Co.
3. Stander: *Williams Obstetrics*, 8 ed., New York, 1941, D. Appleton-Century Company, p. 1060.
4. (a) Goodman: *J. A. M. A.* 57: 1260, 1911.
(b) Rubin: *Surg., Gynec. & Obst.* 13: 625, 1911.
5. Aufeld and Aschoff: *Ztschr. f. Geburtsh. u. Gynäk.* 51: 544, 1904.
6. Adsell and Seidenstein: *Proc. Soc. Exper. Biol. & Med.* 32: 931, 1935.
7. Westman: *J. Obst. & Gynaec. Brit. Emp.* 44: 821, 1937.
8. Westman: *Acta obst. et gynec. Scandinav.* 5-7 (Sup. No. 3), 1929.
9. Lewis and Hartman: *Contribution to Embryology*, Carnegie Institution of Washington, No. 143, 24, 187, 1933.
10. Hertig, A. T., and Rock, J.: *AM. J. OBST. & GYNEC.* 44: 973, 1942.
11. Stander: *Williams, Obstetrics*, 8 ed., New York, 1941, D. Appleton-Century Co., p. 1059.
12. Cited in detail by Devreigne: *L'Ostetrique* 16: 959, 1911.
13. Franz: *Verhandl. d. deutsch. Gesellsch. f. Gynäk.* 8: 214, 1899.
14. Pankow: *Hegar's Beitr.* 15: 23, 1910.
15. Jaschke: *Ztschr. f. Geburtsh. u. Gynäk.* 67: 659, 1910.
16. Tiegel: *Ztschr. f. Geburtsh. u. Gynäk.* 77: 399, 1915.
17. Reinhardt: *Zentralbl. f. Gynäk.* 48: 1490, 1924.
18. Baccialli: *Riv. ital. di ginec.* 5: 1, 1927.
19. Gansbauer: *Zentralbl. f. Gynäk.* 51: 1393, 1927.
20. Meyer: *Finska läk. sällsk. handl.* 71: 177, 1929.
21. Kleiner: *Monatschr. f. Geburtsh. u. Gynäk.* 83: 291, 1929.
22. Cousse: *Ann. L'Inst. Chir. de Bruxelles* 35: 1, 1934.
23. Schürger: *Zentralbl. f. Gynäk.* 61: 2584, 1937.
24. Desirotte: *Bruxelles méd.* 27: 802, 1940.
25. Connors, D. A., Cresci, J. V., and Glass, M.: *AM. J. OBST. & GYNEC.* 45: 309, 1943.
26. Wolters: *Zentralbl. f. Gynäk.* 48: 672, 1924.
27. Baccialli: *Riv. ital. di ginec.* 6: 362, 1927.
28. Tropea: *Rassegna d'ostet. e ginec.* 38: 93, 1929.
29. Bolaffi: *Riv. ital. di ginec.* 15: 517, 1933.
30. Hyslop: *Brit. M. J.* 2: 1256, 1935.
31. Iolkin: *Zentralbl. f. Gynäk.* 50: 3071, 1926.
32. D'Aprile: *Clin. ostet.* 39: 14, 1937.
33. Wittrin: *Zentralbl. f. Gynäk.* 62: 346, 1938.
34. Reist: *Monatschr. f. Geburtsch. u. Gynäk.* 112: 65, 1941.

THE ROLE OF THE INTERMITTENT CONTRACTIONS OF THE UTERUS IN THE PROCESS OF LABOR

Observations Made With the Lóránd Tocograph

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IT IS taken for granted universally that the intermittent contractions of the uterus are essential to the process of labor. And included in this assumption is the belief that they probably play a role in the advancement of the first, as well as in that of the second stage of labor. No doubt the first of these opinions is based largely upon the further supposition that intermittent contractions invariably accompany labor, and to a less extent on the observation that prolonged labors, not due to disproportion, are accompanied by contractions of poor quality.

Certain observations upon the motility of the uterus during labor, made with the tocograph, are of interest in connection with the above considerations.

Observations

Among the tracings of the uterine activity secured from some 1,800 patients when in labor, we possess the records of two individuals who experienced no intermittent contractions. These two observations are as follows:

Absence of Intermittent Contractions During Labor in Association With Abruptio of the Placenta

CASE 1.—Fig. 1 reproduces the tocographic records of a patient who was experiencing an abruptio of the placenta during labor; the details of this experience have been described previously.¹ Although this patient exhibited no detectable intermittent contractions after the abruptio of her placenta had taken place, she delivered her infant spontaneously per vaginam. Her uterine tone, however, was unusually high throughout labor, and no doubt it was the existence of this high tone that made it possible for the labor to proceed.

Absence of Intermittent Contractions During a Normal Labor

CASE 2.—Mrs. R. J., a colored primipara, aged 28, had an uneventful pregnancy except for a slightly excessive gain in weight. Her pelvis was of normal size, and her expected confinement date was November 2, 1943.

Her membranes ruptured spontaneously without pain at 4 P.M. on November 14, and she was admitted at once to the hospital. Her uterus was unusually tense, but was exhibiting no intermittent contractions.

The fetus presented in the R.O.T. position; the head was engaged and the cervix was dilated 8 to 9 centimeters.

Pain began at 7 P.M. November 17. This was described as a belt of pain below the umbilicus, beginning in the back and radiating forward. It was described further as being intense and deep. It would ease slightly at times sufficiently for her to get her breath, and increase again immediately, but was never absent. This was the only painful sensation which she experienced. After her labor, the patient volunteered the statement that she believed that she had never experienced true labor pains as they had been described by friends.

Tracings #2,094-2,098

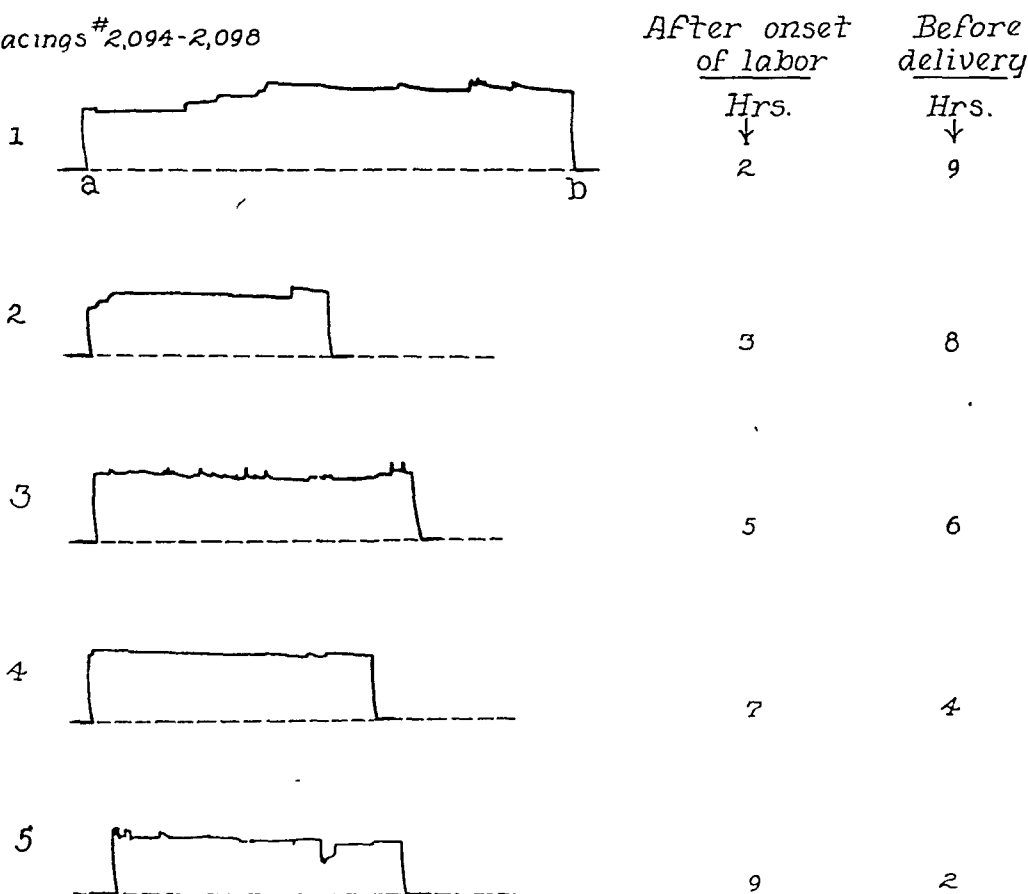


Fig. 1.—Showing the uterine motility throughout labor of a patient experiencing abruption of the placenta. Observations recorded through the medium of the abdominal wall by means of a Lóránd tocograph. Machine placed on abdomen at A end of each tracing and removed at B end. Note absence of intermittent contractions, but unusually high tone which is indicated by height of graphs above their base lines.

The uterus remained uniformly and unusually tense for 40 hours, and exhibited no palpable intermittent contractions during long periods of continuous observation. A series of tocographic records, reproduced in Fig. 2, was secured at irregular intervals during this period. None of these tracings reveals the presence of any intermittent contractions.

The amniotic fluid became discolored. Vomiting occurred repeatedly, and the patient's temperature rose. In view of her general condition, and because the fetus failed to progress, delivery was decided upon.

The patient took her anesthetic poorly, becoming cyanotic. At this time the fetal heart sounds disappeared. The cervix hung loosely around the infant's head, which was in midpelvis in the transverse

diameter, and presented considerable molding and caput formation. Forceps were applied within the cervix and the infant was delivered without incident. It was stillborn and weighed 3,785 grams.

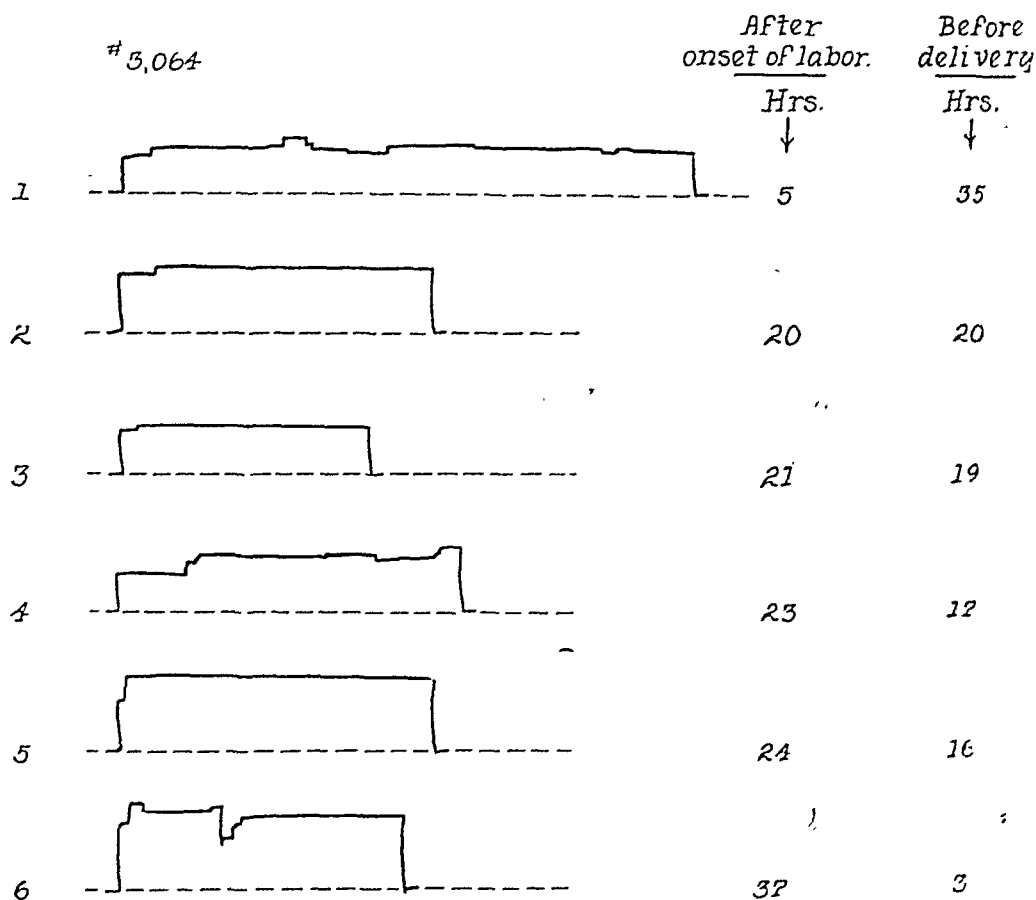


Fig. 2.—Showing the uterine motility throughout labor of a patient who experienced neither subjective nor objective evidence of the presence of intermittent uterine contractions. Note unusually high uterine tone.

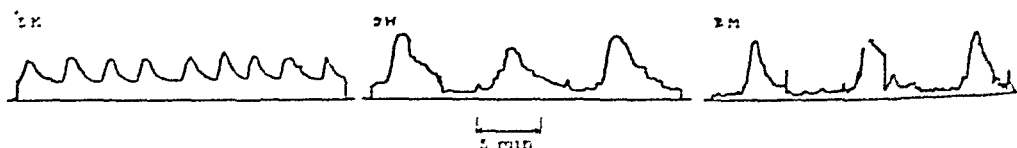


Fig. 3.—Examples of the intermittent contractions of three individuals made during the first stage of their labors. Tracing E. K. illustrates normal uterine tone and intermittent contractions which are normal with respect to: (a) frequency, (b) strength, and (c) duration. The tracings of patients S. W. and E. M. reveal a lower tone than normal. Their contractions are very much stronger than normal, and also less frequent and longer in duration than normal.

The Influence of the Contractions Upon the Duration of the First Stage of Labor

The magnitude of the uterine contractions which takes place during labor, as a rule, does not differ greatly from patient to patient. The occasional individual, however, may experience contractions of unusual strength.

Fig. 3 reproduces the tocographic tracings of three individuals taken during the first stages of their labors.

Patient E. K. (Fig. 3), was a primipara who had a labor of 27 hours' duration. Her second stage consumed 1 hour and 10 minutes. Her

tracings were made 7 hours before delivery, when the cervix was dilated only 5 centimeters. This tracing registers a normal tone and contractions which were normal in all respects. Her delivery, likewise, was normal.

Patient S. W. (Fig. 3), was a para x. Her labor lasted 12½ hours. This tracing reveals a low uterine tone, but extremely strong contractions of unusually long duration, occurring relatively infrequently. Her tracing was made 11 hours before delivery, when her cervix was dilated only 2 centimeters. The second stage of labor was short requiring less than 20 minutes.

Patient B. M. (Fig. 3), was a para v, who experienced a labor of 38 hours' duration. Her tracing was made 11 hours before delivery, when her cervix was only dilated 3 centimeters. She, likewise, had unusually powerful contractions throughout labor. The second stage of labor was short lasting less than 40 minutes.

Comments

It is quite true that labor almost universally is accompanied by intermittent contractions. The present observations, however, indicate that it may proceed to completion in the absence of such contractions. For this to take place, however, the uterine tone must be persistently high. We have never observed labor to occur in the absence of both intermittent contractions and a persistently high uterine tone.

The first stages of the two labors associated with unusually strong contractions were of average length.

The present observations thus suggest that the intermittent contractions are not indispensable to the process of labor, and that they do not play a significant role in determining the length of the first stage of labor.

In view of these findings, it would seem that any efforts to be expended in initiating labor, or in improving labors of poor quality, should be directed primarily at some more fundamental purpose than in merely trying to influence the power of the uterus to contract intermittently. Toward just what goal future researches should be directed in order to acquire a better understanding of the mechanism of labor, remains to be determined.

Reference

1. Murphy, D. P.: AM. J. OBST. & GYN. 44: 694, 1942.

THE PREVENTION OF CANCER OF THE CERVIX

Report of Second Survey

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IN 1941, a report¹ was published on a survey of 10,000 cases of deep cauterization of the cervix in the Elizabeth Steel Magee and St. Francis Hospitals, Pittsburgh, Pa. This survey covered a period of twenty-five years and was finished in 1939. Before the survey, it was our clinical impression that this procedure has been effective in preventing cancer of the cervix. In the follow-up study, 3,143 replies to a questionnaire were received. Pelvic examinations were done in 1,341 of the patients. An effort was made to find out the cause of all deaths that occurred in the series, and the nature of all secondary operations. There were two known cases of cancer of the cervix following cauterization before the survey was started, and one of them is still alive. The extent of the cauterization was questionable in both of these cases.

In this first survey no other cases of cancer of the cervix were found. In an effort to determine the number of cases of cancer that should have occurred in this group, we were unable to get definite information from published statistics, or from the various cancer societies and other sources of information. We were referred to Dr. Levin,² whose work in this field has been outstanding and our follow-up material was turned over to him for evaluation. He estimated the expected number of deaths from uterine cancer by applying to each age group, for the period of observation, the mortality rates among women in Pittsburgh for the census year 1930. He found in the survey that the average age of the patients contacted, or who had died, was 40.1 years, and that the average period of observation was only 5.6 years. It was evident then that the largest number of the patients contacted has been operated on in more recent years. He stated that if the 3,143 patients were observed until all had died, 79 deaths from uterine cancer would be expected. Whereas, in our limited survey only 6 deaths could be expected. He stated that our follow-up carried us to the age level where cancer of the cervix should rise in incidence rapidly, and he recommended further follow-up study. In the first questionnaire, information was requested as to patient's general health and the presence of vaginal discharge or bleeding, without stating the purpose of the study.

Second Survey

In the second survey, we were more specific and explained that an attempt was being made to find out if the operation had succeeded in

preventing cancer of the cervix. This brought many more replies. Many other patients, whose letters had been returned in the first survey because of inaccurate address, were located by means of the city directory. So we now have a follow-up of 4,487 patients. No other cases of cancer of the cervix were found. The material from this survey was submitted to Dr. Levin² again, and we quote from his first report:

"Analysis of the tabulated results of your follow-up series shows some interesting facts. The mean age at time of first operation was 34.4 years; at time of last observation it was 42.8 years (Table I). The average period of observation was 8.7 years. Although this is still a comparatively youthful group of patients, the findings with respect to cancer are fairly striking.

TABLE I. AGE-DISTRIBUTION AT TIME OF CAUTERIZATION AND AT TIME OF FOLLOW-UP SURVEY: PATIENTS TREATED BY DEEP CAUTERIZATION OF CERVIX UTERI 1914 TO 1939

AGE GROUP (YEARS)	NUMBER IN EACH AGE-GROUP		PERSON-YEARS OBSERVATION*
	AT OPERATION	AT LAST OBSERVATION	
14	8	0	4.00
15 to 19	170	12	447.50
20 to 24	580	116	2,068.75
25 to 29	864	345	4,609.75
30 to 34	899	633	6,556.25
35 to 39	769	762	7,208.75
40 to 44	583	802	6,656.75
45 to 49	351	696	5,219.75
50 to 54	178	570	3,348.75
55 to 59	47	297	1,713.75
60 to 64	27	149	781.25
65 to 69	8	73	308.75
70 to 74	2	20	100.00
75 to 79	1	8	37.50
80 to 84	0	3	12.50
85 to 89	0	1	2.50
	4,487	4,487	39,076.00
Mean age	34.31 ± .14	42.82 ± .15	
Mean years observation per person—8.71			

*Calculated separately from the following information: For each age-group, the numbers (a) cauterized, (b) died, (c) carried over from earlier ages, (d) carried into the next age-group, (e) observation ended by follow-up.

On the basis of cancer mortality among the female population of Pennsylvania in 1930, we calculated the number of cases of cancer of the breast, fundus uteri and cervix uteri which would be expected among the total series of 4,487 women during the period of observation. For each type of cancer the expected number of cases was estimated according to whether deaths per year are considered to represent 80 per cent of new cases or 50 per cent, giving both a low and a high value for expected cases. The figures are:

	Expected Cases	Observed Cases
Breast cancer	10.7 to 17.2	18
Uterine fundus cancer	3.3 to 5.4	4
(excluding hysterectomies)	2.5 to 4.2	
Uterine cervix cancer	14.5 to 23.2	2

The number of cases of breast cancer and uterine fundus cancer which was found agrees quite well with what would be expected. The number

of cervix uteri cases is about one seventh that expected, representing a reduction of approximately 85 per cent.

In considering the significance of these findings, a number of complicating factors must be considered. The expected number of cancer cases refers to what would be expected if these women were comparable in all respects to the average female population of Pennsylvania. Actually, the series differs in several respects from the general female population, and one must ask whether these differences could be responsible for the results obtained. With respect to color and marital status, the 'cauterized series' probably had a higher proportion of colored women and certainly a higher proportion of married women than would a random sample of women of the same age distribution in Pennsylvania. However, the effect of both these factors would be to *increase* the expected number of cervix cancer cases. They may, therefore, be disregarded, although it would be interesting to have exact data on color and marital status, by age, at time of first and last observation.

The chief difficulty in a follow-up study where the follow-up is incomplete is to be certain that the followed cases have not been favorably selected. For example, the follow-up series *was* favorably selected with respect to death, probably because there was less chance of hearing from or about a dead patient. The question is whether, for some unknown reason, we were *less* likely to hear from a patient with cervix cancer and *more* likely to hear from a patient with breast cancer. I can see no reason to believe this. In fact, it seems to me that the form of cancer which a gynecological service would be *most* likely to hear about, would be uterine cancer.

There are a few more calculations and tabulations which we hope to make on your material. In any event, I believe that this material as it stands should be reported. Perhaps some detail regarding the method of calculation might be of interest to others engaged in similar follow-up studies."

It will be noted that Dr. Levin has been very conservative in his estimates, for in the series he found our incidence of cancer of the breast equal to the upper estimate of expected cancer and the observed cancer of the fundus equal to the mean estimate. But in cancer of the cervix, he compares the known incidence with the lowest figures of expected incidence or 14.5 cases. Dr. Levin later wrote as follows:

"After writing you last, it occurred to me that there was a valid objection to using the *living* cases of cancer observed in your follow-up, in comparison with the expected number of cases or deaths. The reason is that the method of follow-up by questionnaire tends to *select* living patients, because obviously a living patient is more apt to "answer" a questionnaire than a dead one. This is borne out by the fact that the number of deaths from all causes which the follow-up uncovered was only about half the expected number. For that reason, I believe we are on safer ground in confining attention to deaths, in making our comparisons.

The expected deaths from various causes were calculated by applying the age-specific mortality rates for Pennsylvania (females) in 1930. This year was selected both because of the accuracy of the rates in a census year and because 1930 was close to the middle year of the observation period (1914 to 1939).

TABLE II. EXPECTED AND OBSERVED DEATHS FROM VARIOUS CAUSES, AMONG 4,487 PATIENTS FOLLOWED FOR VARYING PERIODS AFTER DEEP CAUTERIZATION OF THE CERVIX

CAUSE OF DEATH	NUMBER OF DEATHS		RATIO: OBSERVED EXPECTED
	OBSERVED	EXPECTED*	
All causes	156	297.3	0.52
All cancer	26	44.9	0.58
Cancer of the fundus uteri†	1	2.0	0.50
Cancer of the cervix uteri‡	1	11.6	0.09
Cancer of the breast	11	8.3	1.32

*Deaths expected on basis of age-specific mortality rates among all females, Pennsylvania, 1930, applied to the person-years observed in each age group.

†Patients who had hysterectomy were not counted as exposed to risk of developing carcinoma of the fundus.

‡Patients who had total hysterectomy were not counted as exposed to risk of developing carcinoma of the cervix.

You will note, from Table II, that the number of deaths from 'all causes' observed was almost half the expected. The number of deaths from 'all cancer' observed was in approximately the same ratio. The inference is that the method of follow-up was as successful in tracing deaths from cancer as deaths from any other cause.

Considering now the deaths observed from cancer of various sites, we may compare these with the calculated expected deaths in two ways: First, on the assumption that the deaths which were traced were actually all the deaths which occurred; second on the assumption that the follow-up missed the same proportion of deaths from cancer as it did deaths from all causes. In Table III, both of these comparisons are made.

TABLE III. EXPECTED AND OBSERVED DEATHS FROM CANCER OF VARIOUS SITES AMONG 4,487 WOMEN FOLLOWED AFTER CAUTERIZATION OF THE CERVIX

SITE OF CANCER	EXPECTED* (T)	OBSERVED (O)	OBSERVED† "CORRECTED", (O)*	VALUE OF P‡ FOR	
				T-O	T-O†
Cervix	11.6	1	2	0.002	0.005
Breast	9.2	11	21	0.59	0.0004
Stomach	5.8	1	2	0.05	0.11
Intestines, rectum and anus	4.9	3	6	0.39	0.62
Other sites	15.0	10	19	0.20	0.30

*Calculated from age-specific mortality rates among all females, Pennsylvania, 1930, applied to person-years observation in each age-group of the 4,487 women.

†Corrected by assuming that the actual number of deaths was in the same ratio as $\frac{\text{Expected Deaths from all causes}}{\text{Observed Deaths from all causes}} = \frac{297.3}{156} = 1.906 \times \text{observed deaths}$.

‡P = states the probability that the difference between expected and observed values would occur as a result of sampling error. Conventionally, values of P of 0.05 or greater are interpreted as indicating that random error could account for the difference found.

In the first comparison, only deaths from cervix cancer appear to be strikingly different (less) than expected. In the second comparison, deaths from cervix cancer are still significantly low, but, in addition, it appears that deaths from breast cancer were significantly higher than expected. As far as cervix cancer is concerned, even if we count the additional living case which was observed as dead and thereby raise the 'corrected observed' number of deaths to 4, the decrease is still greater than can be accounted for by sampling variation ($P = 0.0264$).

The decrease in deaths (and cases) of cervix cancer in this series becomes all the more striking when one considers that these are the cases which a gynecological clinic would be least apt to miss, in comparison to other forms of cancer, or other types of fatal illness.

This group of women differed from the general female population of Pennsylvania in the following particulars:

- (1) More married women—93.0 per cent as compared to 65.7 per cent for this age distribution.
- (2) All had some pre-existing gynecological disease.
- (3) More women of the lower income group ('clinic class').
- (4) More Negroes.

Each of the above factors should operate to produce even more cervix cancer in this group than in the average female population. To this extent, therefore, the discrepancy between observed and expected deaths from cervix cancer may be even *greater* than shown by our analysis.

As far as I know, there is no published study in which the question of the prophylactic value of cauterization has been carried as far toward a final definitive answer as yours. The data you have collected are consistent with the hypothesis that cauterization reduces the subsequent incidence of cervix cancer, although it does not provide the final and unequivocal evidence which would be desirable.

I still feel that these results should be made known. I also feel that you should continue this investigation. I would be glad for the opportunity to discuss in greater detail the question of further investigation and analysis of your material."

It must be emphasized that these results were obtained by *deep* cauterization of the cervix, the technique of which was published again in 1941.³ It is a much more extensive cauterization than is usually done, and the purpose is the destruction of all glands and infected mucosa in the cervix. No aftertreatment is necessary when it is followed by subtotal hysterectomy, but in all other cases, office dilatations with uterine dressing forceps must be carried out to prevent stricture of the cervix. These dilatations are done four, six, eight and ten weeks after operation and again in six months. Anyone who is not willing to carry out these irksome postoperative dilatations should not use this type of cauterization except when hysterectomy is done.

There has been no similar follow-up study of a series of light cauterizations of the cervix so that I am unable to make comparisons as to the relative value of the two procedures in the prevention of cancer. But it is significant that there are no known cases of cancer of the cervix in our own personal series. The two cases that occurred had been cauterized by surgeons when they first adopted this method of cauterization, and one of them volunteered the information that the cervix of his patient was not cauterized to the same extent as is practiced by him now. If chronic infection is a factor in the production of cancer, deep cauterization would seem to be a more logical procedure than superficial cauterization.

It has been stated in the literature that cauterization of the cervix may eliminate cervicitis, but that it could hardly prevent cancer because 80 per cent of cervix cancer develops from the squamous cells of the vaginal portion of the cervix. It is our contention that cancer of the cervix rarely, if ever, develops from normal squamous epithelium but

that it develops at the junction of squamous epithelium and the chronic inflammation of cervicitis either on the surface of the portio or perhaps in metaplasia in the glands, and that if the cervicitis is eliminated, cancer of the cervix will be eliminated practically. Equally fallacious is the argument that cancer of the stump after supravaginal hysterectomy may occur in a normal cervix, based on the fact that the cervix appeared normal at the time of hysterectomy. Masson⁴ writes: "It is known that cervicitis is a very common sequel to subtotal hysterectomy. In more than 500 cases, cervicitis with leucorrhea was sufficient to require treatment after subtotal hysterectomy. In many of these cases there was no history of leucorrhea before the body of the uterus was removed." It has been my observation also that a cervix which appears to be normal at the time of hysterectomy may be definitely inflamed on examination months or years later. This is probably the result of circulatory changes, in a glandular structure, which predispose to infection, for if the glandbearing portion of the cervix is excised or destroyed with the cautery as the first step in hysterectomy, no subsequent cervicitis develops.

I will repeat with a few alterations, the following paragraphs of the previous report:

"Perhaps there is no method of preventing cancer of the cervix one hundred per cent, but in our personal series, we have been unable to find a single case and in the entire series of 10,000 cases in two large hospitals, only 2 cases are known to have occurred. A larger series of cases or a longer period of time and a better follow-up may change that report. Even so, if it is shown that the incidence of cancer has been much reduced, the work has been worth while. It is much more satisfactory than a cure of an equal number of cases of cancer of the cervix for many of the cancer cured cases are uncomfortable and unhappy; uncomfortable from undesirable radiation effects, and unhappy because of the dread of recurrence. Our interest has been in the prevention rather than in the cure of cancer of the cervix in the advanced stages in which it is usually seen today.

"Prevention of cancer of the cervix by any method that is effective is advocated in this paper. Deep cauterization has been the method used in this series because it can be done quickly, along with other operative procedures, and microscopic sections show that it is effective in eliminating cervicitis."

Conclusions

1. Chronic cervicitis seems to be a contributing factor in the causation of carcinoma of the cervix.

2. Cancer of the cervix is insidious in onset and because of the late stages in which it is seen today, prevention of cervicitis, prevention of cancer by adequate treatment of existing cervicitis, and early diagnosis by periodic examination of women over 25 years of age, offer the best solution of the problem.

3. In order to destroy infection in the cervix by cauterization, it is often necessary to cauterize deeply and extensively.

4. Careful postoperative care and treatments are necessary to prevent stenosis of the cervical canal after deep cauterization when the uterus is not removed.

5. As far as we know, deep cauterization of the cervix has been an effective method of preventing cancer in our series of 10,000 cases, for only 2 cases of cancer of the cervix are known to have occurred in this series.

6. In the second follow-up study, the average time interval after cauterization was 8.7 years, and the average age of the patient 42.8 years. The results show approximately 80 to 85 per cent reduction in the incidence of cancer, or in deaths from cancer of the cervix in the group followed for by a new application of a statistical method to our series of 4,487 followed patients, Levin estimates the expected incidence as 14 to 23 cases of cancer of the cervix in the time observed. Two cases are known to have occurred before the survey, and one of them died from cancer of the cervix, when 11.6 deaths would be expected.

References

1. Cashman, B. Z.: The Role of Deep Cauterization in the Prevention of Cancer of the Cervix, *AM. J. OBST. & GYNEC.* 41: 216-224, 1941.
2. Levin, Morton L.: Associate Director, Division of Cancer Control New York State Department of Health, Albany, N. Y. Personal Communication.
3. Cashman, B. Z., and Frank, John S.: Deep Cauterization of the Cervix—A Factor in Reducing the Mortality of Hysterectomy, *AM. J. OBST. & GYNEC.* 41: 379-390, 1941.
4. Masson, James C.: Total vs. Subtotal Hysterectomy, *Am. J. Surg.* 48: 255, 1940.

AN ANALYSIS OF THE EFFECTS OF CONTINUED THIOUREA TREATMENT IN PREGNANCY AND ON THE DEVELOPMENT OF THE OFFSPRING IN THE RAT*†

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THIOUREA and thiouracil have been used successfully in the treatment of hyperthyroidism in the human.¹⁻⁶ Since pregnancy may often be complicated by hyperthyroidism⁷ the question as to whether such drugs can be used with impunity to alleviate this condition in the gravid animal becomes an urgent one. Possible effects of the administration of these agents on the fetus and the development of the offspring must also be considered.

The consensus is that these agents act in the manner of a chemical thyroidectomy by preventing the formation of the thyroid hormone.^{8, 9} Thyroidectomy in the immature animal has long been known to be followed by a retardation of growth (sheep and goats,¹⁰⁻¹¹ rabbits,¹² rats¹³⁻¹⁵). More recently Salmon^{16, 17} and Scow¹⁸ have reported that removal of the thyroid one to three days after birth results in a marked retardation of growth and maturation of the rat.

We have already reported¹⁹ that thiourea administered to pregnant animals produces a marked hyperplasia of the thyroid glands in the suckling young. Hughes²⁰ has recently given some information on the effects of thiouracil on the growth of young rats. The present paper furnishes further details concerning the effects on the offspring of thiourea treatment during and after pregnancy.

Methods

At intervals of 0 to 22 days prior to parturition, pregnant rats of an inbred hooded-Wistar strain were placed on a laboratory stock diet containing 0.5 per cent thiourea. Following delivery, all litters were reduced to 6 animals. After weaning from their thiourea-treated mothers, the young rats obtained the drug directly from the thiourea diet. Several of these animals were maintained on this ration for periods of 13 to 157 days, and were then placed on the stock laboratory diet. In several cases, some of the litters were divided immediately after delivery so that some of the young were left with their treated mothers, whereas their litter mates were placed with untreated lactating females.

*Aided by a grant from The Elizabeth Thompson Fund.

†Acknowledgment is made to Mr. Albert Stenger for technical assistance.

Selected animals were sacrificed, the thyroid glands and a number of other organs were weighed rapidly and fixed in Bouin's or Helly-Zenker's solution. Where the thyroids were too small to be dissected without injury, a portion of the trachea with the glands attached was removed and fixed in Bouin's fluid.

TABLE I. EFFECT OF THIOUREA TREATMENT UPON RAT AND THYROID WEIGHT

CASE NO.	AGE DAYS	NO. OF ANIMALS	NO. OF DAYS ON T.T.*		TOTAL DAYS ON T.T.*	STOCK DIET IN DAYS AFTER T.T.	MEAN BODY WT. GM.	MEAN THYROID WT. MG.	MEAN THYROID WT. MG./100 GM. BODY WT.
			PRE- PARTUM	POST PARTUM					
45-1	21	2	0	21	21	0	30	14	46
45-2	24	3	0	24	24	0	37	19	51
46-1	10	4	0 to 1	10	10 to 11	0	14	5	35
30-1	4	1	4	4	8	0	10	†	--
30-2	8	2	4	8	12	0	17	5	29
30-3	11	2	4	11	15	0	21	7	35
30-4	15	1	4	15	19	0	36.5	10	28
B45	4	2	6	4	10	0	6.5	†	--
47	0	2	7	0	7	0	5	†	--
29-1	1	2	9	1	10	0	5	†	--
29-2	6	2	9	6	15	0	8.5	4	47
29-3	10	2	9	10	19	0	15.5	5	33
41-1	0	3	10	0	10	0	5	†	--
41-2	13	2	10	13	23	0	21.5	6	28
41-3	30	1	10	13	23	17	73	7	9
43-1	0	2	15	0	15	0	4	†	--
43-2	19	2	15	0	15	19	30	4.0	13
43-3	36	2	15	0	15	36	89	9.5	11
38	86	2	22	86	108	0	50	50	100
36-40	222	3	4	157	161	65	200	60	30
36	264	2	4	264	268	0	130	†	--

*Thiourea treatment.

†Thyroid fixed on trachea.

‡Animals still alive.

Results

Growth.—The feeding of 0.5 per cent thiourea incorporated in the laboratory ration to pregnant rats for 1 to 15 days prior to parturition produced neither visible effects upon the external appearance of the offspring, nor upon the size of the litters. The weights of the newborn from 9 litters of treated animals averaged about 5 grams as did newborn animals delivered by normal untreated mothers.

Continued thiourea treatment via the mother and after weaning through the diet resulted in signs of retardation of growth by the tenth

to the twenty-fifth day of age. The treated rats reached a growth plateau at variable times such as 85, 100, and 157 days of age.

After 157 days on the thiourea diet (Case 36), 4 males averaged 120 Gm., and 2 females 105 grams. The litter was divided so that 2 males averaging 124 Gm. and one 105 Gm. female were left on the experimental diet, and 2 other males averaging 116 Gm. and a female weighing 104 Gm. were placed on the ordinary laboratory ration. Forty days later,

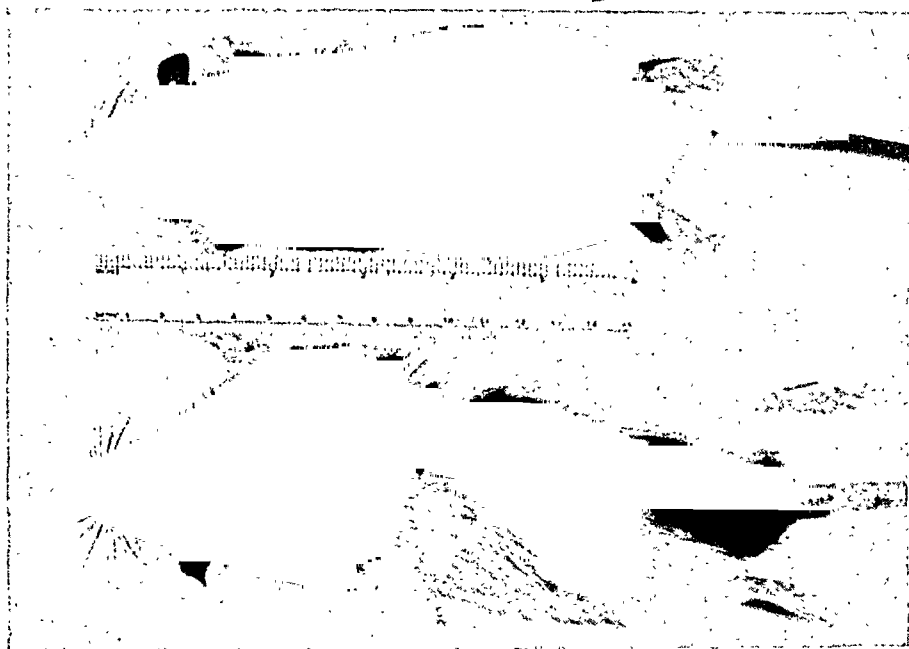


Fig. 1.—Reversibility of thiourea effect (litter mates). Black rat (wt. 125 Gm.) on continuous thiourea treatment for 210 days (4 days prepartum); hooded rat (220 Gm.) on continuous treatment for 161 days and then on normal diet for 49 days.



Fig. 2.—Thiourea and growth. 84-day-old thiourea treated animal (50 Gm.) as compared to an untreated animal (160 Gm.) of the same age. The cretin was obtained from a mother treated with thiourea for the entire gestation period.

this latter group showed an average gain of 72 Gm. for the males, and of 41 Gm. for the female. They continued to grow and after 65 days on the normal diet, the males averaged 210 Gm. and the female weighed 180 grams. The males which had been continued on the drug for 55 additional days averaged 126 Gm., and the female remained at 105 grams. The males now 264 days old (107 days since the litter was segregated) average 130 Gm. in weight (Fig. 1).

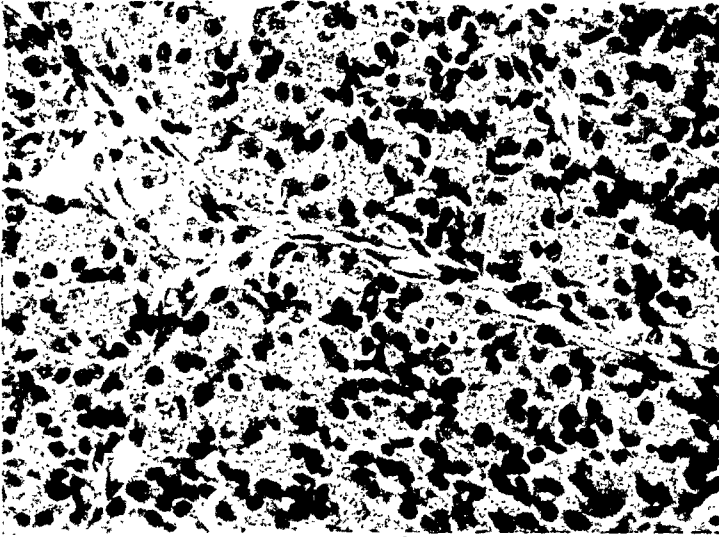


Fig. 3.—One-day-old rat obtained from a mother treated with thiourea for the last 10 days of the gestation period. Note the marked hyperplasia and absence of colloid as compared with that in Fig. 4.

Figs. 3 through 9 are photomicrographs of sections through the thyroid glands of thiourea-treated and normal rats, fixed in Bouin's fluid and stained with hematoxylin and eosin. (×408.)



Fig. 4.—One-day-old rat obtained from untreated mother.

In Case 38, a female which had been treated throughout the entire gestation period gave birth to 2 serawny female young. Treatment was continued and they developed at a greatly retarded rate showing the definite cretin characteristics described by Hughes. At the age of 84

days, one weighed 50 Gm., and the other 78 Gm. (Fig. 2). At this age, our control female rats averaged 160 Gm. and control males, 235 grams.

The Thyroid Glands.—The effectiveness of the pre- and postpartum treatment on the thyroid gland is presented in Table I. The data here disclose that the thyroids of all treated animals range from 28 to 100 mg. of gland per 100 Gm. of body weight. Untreated adult controls of our colony average 8 mg. of thyroid, and our untreated 12 to 18 Gm. animals average 16 mg. of thyroid per 100 Gm. of body weight.

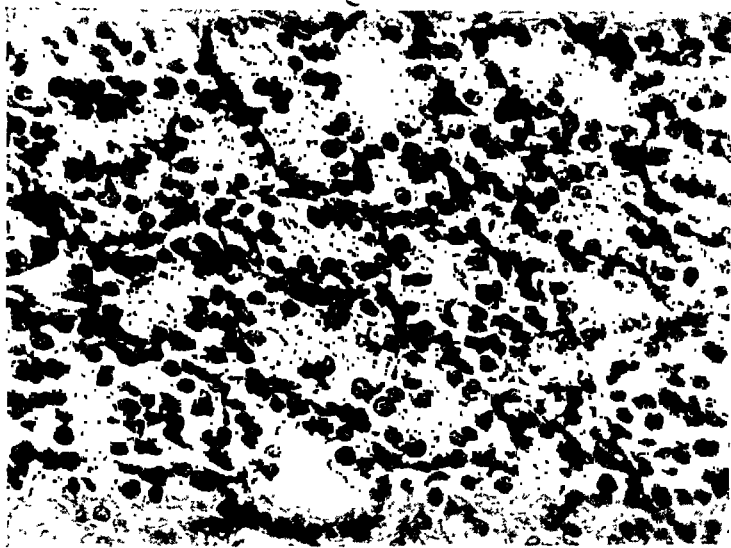


Fig. 5.—Ten-day-old rat obtained from a mother put on a thiourea-containing diet on the day of delivery. Note the higher epithelium and scantier colloid than that in Fig. 6.

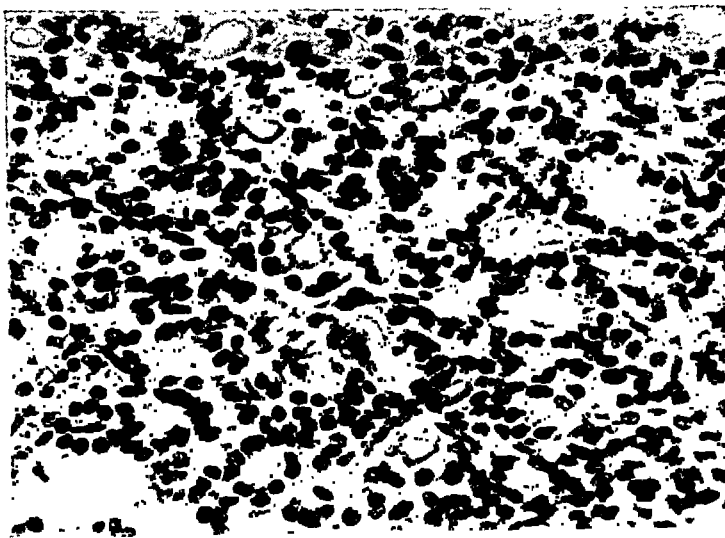


Fig. 6.—Ten-day-old rat obtained from untreated mother.

Several mothers were placed on the thiourea-food 7 (Case 47), 10 (Case 41-1) and 15 (Case 43-1) days prior to parturition. A number of the young were sacrificed at birth, and the glands were fixed attached to the trachea. Macroscopically, the glands appear enlarged and hyperemic. Microscopic examination of the glands reveals some irregularity in the follicles, high columnar epithelium and limited amounts of lightly

staining colloid (Figs. 3 and 4). An histologic study of the thyroids of 10 (Case 46-1) and 21 (Case 45-1) days-old rats nurtured by mothers which had been placed on the thiourea diet on the day of delivery disclose a similar picture (Figs. 5 and 6). Continued treatment resulted in an increase in the weight of the glands as has been established by Mackenzie,²¹ Astwood¹ and others.

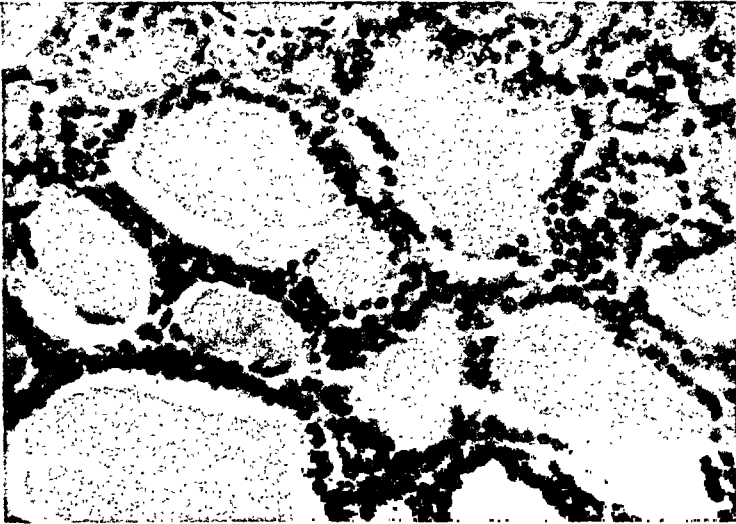


Fig. 7.—Result of thiourea treatment for 161 days followed by normal diet for 65 days. Epithelium is low, approaching the normal picture, and large amounts of densely staining colloid are present.

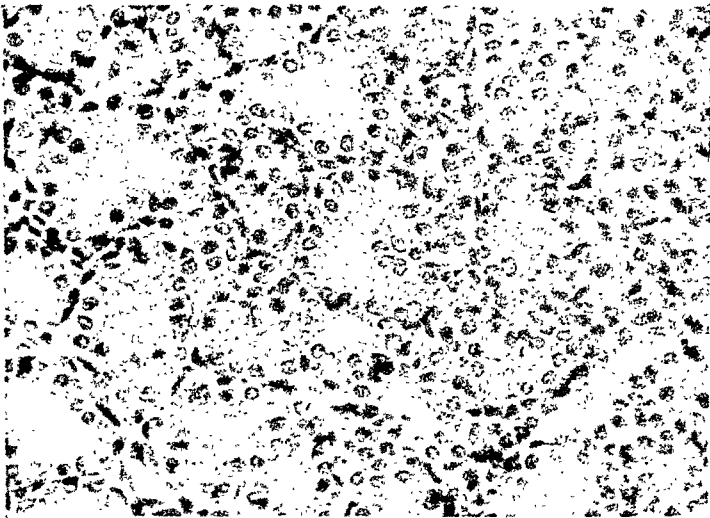


Fig. 8.—Thirteen-day-old litter mate to animal whose thyroid is shown in Fig. 3. Result of ten days of prepartum and 13 days postpartum treatment. The gland is highly active.

It is of interest to note that several rats (Case 36-40) which had been treated for 161 days and then placed on a normal diet for 65 days still possessed large thyroid glands, 30 mg./100 Gm. of rat as compared with 8 mg./100 Gm. for our untreated controls. The histologic picture, however, was that of a normal gland (Fig. 7). Examination of Table I discloses several instances in which short term exposure to thiourea (Case 41-3, 23 days) followed by a return to a normal diet for 17 days

resulted in a reduction in the rate of growth of the gland, and a return to the normal histologic picture (Figs. 8 and 9).

Reproduction.—Mixed litters of our animals maintained on thiourea from the time of birth or prior to it have been observed for 7 months, but none has delivered offspring.

In one instance (Case 39), 6 litter mates (5 females and 1 male) had been kept in one cage on a thiourea ration until they were 100 days old. At this time, the litter was divided and 3 of the females averaging 89 Gm. were transferred to another cage and placed on a stock diet. The male (110 Gm.) and the other female (97 Gm.) were left in the experimental cage. Twenty-one days after being placed on the normal diet, the largest of the females (126 Gm.) delivered 3 healthy young.

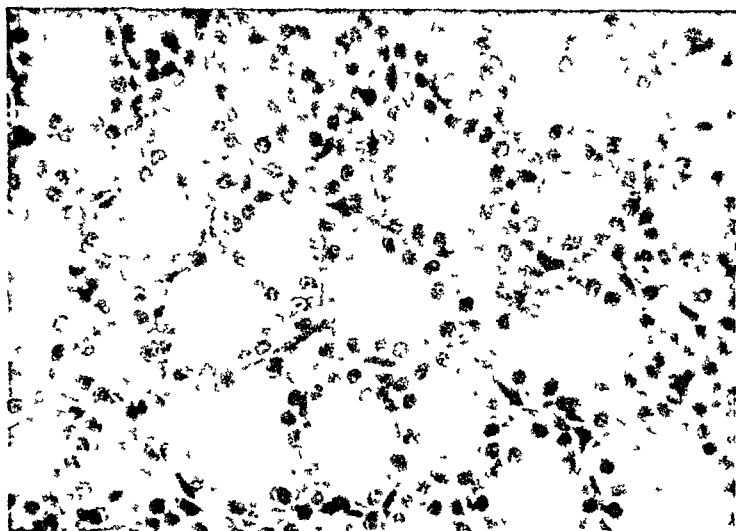


Fig. 9.—Thirty-day-old litter mate to animals whose thyroids are shown in Figs. 3 and 8. Result of return to normal diet for 17 days after a 10-day prepartum and 13-day postpartum treatment. The gland appears normal.

In Case 36, males and females were kept together for 157 days. The litter was divided so that 1 male and 2 females were placed in each cage. Thirty-seven days after being transferred to the normal diet, the 145 Gm. female delivered healthy offspring, and 30 days later external evidences of pregnancy were again visible.

Discussion

The data of the present experiments show that the retarded growth rate and the hyperplastic, activated thyroid glands of young rats, delivered by mothers maintained on a 0.5 per cent thiourea diet during and after pregnancy, were transient in nature. These effects disappeared when the animals were placed on a laboratory stock diet. Administration of the drug in the ration enables one to study the thyroid-developmental mechanism without resorting to surgical thyroidectomy and its attendant hazards. The mortality rate was no higher among our drug-treated rats than among our untreated controls. Hughes²⁰ has reported a high mortality rate in 25- to 30-day-old animals following daily subcutaneous injections of thiouracil. This difference and the

fact that our animals as a rule were heavier and reached the growth plateau at a later date, may be explained in terms of concentration. Thiourea in a dosage of 0.5 per cent of the diet may have been insufficient to produce cessation of all thyroid hormone production.

The presence of active hyperplastic thyroids in young animals carried by thiourea-fed mothers for 7 to 15 days prior to parturition and sacrificed at birth indicates a definite transplacental transmission of the "thiourea" effect. It is not clear as to how this effect is produced, but 3 possible explanations present themselves. One is the passage of the thiourea (molecular weight, 78) through the placenta. Should this be true, then we have presumptive evidence that the thyroid of the fetus is already a functional gland and on being depressed by thiourea calls upon the pituitary to produce thyrotropin. This would further necessitate the postulation of a functional and active fetal pituitary capable of producing a thyrotropic factor. In support of this, is the finding by Fugo and Witschi²² that removal of the hypophyseal primordium in the chick embryo results in the development of a small thyroid gland. Fugo²³ concluded further that the embryonic chick pituitary becomes active during the second half of the incubation period and appears to secrete growth, thyrotropic and gonadotropic hormones. Kull²⁴ has reported that in the albino rat, rapid development of the thyroid gland does not take place until after the eighteenth day in embryonic development, and a fully developed thyroid gland showing follicle and colloid is found only a few hours before birth. The second possibility is that as a result of lowered thyroxine production in the mother, the fetus receives less thyroxine than it would normally, and the pituitary of the fetus responds by sending out increased quantities of thyrotropic factor. The third alternative is that the hyperplasia is brought about by the thyrotropin from the mother.

The last possibility requires that large molecules pass through the placenta from mother to fetus. Ukita²⁵ claimed that thyroidectomy of pregnant rabbits resulted in the prolongation of gestation, incomplete ossification and hypertrophied thyroids in the offspring. These results may be explained on the possible passage of hypophyseal hormone through the placenta. However, in view of the accepted belief that pituitary tropic factors are protein molecules and the scanty evidence in favor of their transplacental passage, opinion must be reserved.

The sole source of thiourea of animals 45-1 and 46-1 (Table I) was their mothers' milk. The thyroid picture was one of extreme activity. Other animals (Table I) which received both pre- and postpartum treatment showed an increase in size and activity of the thyroid directly related to the duration of treatment. In view of the recent findings by Williams, Kay and Jandorf²⁶ (cited by Williams, Weinglass, et al.²⁷) that human milk contains much more thiouracil than any other body fluid, this result is to be expected.

There is thus presented substantial evidence that in the rat an active hyperplastic thyroid gland may be produced directly through the food containing the drug, and indirectly by transplacental and transmammary passage of the effective factor.

The results disclose that those animals which had been on thiourea for periods up to 157 days, and had reached their growth plateaus resumed growth when returned to a stock diet. The histologic structure of the thyroid also returned to normal. In severe animals treated for 4 days prior to birth and 157 days after birth, the thyroid still weighed 30 mg. per 100 Gm. of body weight 65 days after its return to a normal stock diet. The histology, however, was normal. In the light of Astwood's work¹ and our own in vitro and in vivo studies with adult rats,²⁸ the return to the normal condition is to be expected.

In rats completely surgically thyroidectomized,^{17, 29} repair of the thyroidectomy changes in the pituitary did not occur when thyroid therapy was delayed beyond 40 days. Severinghaus²⁹ concluded that a rat completely thyroidectomized at birth becomes physiologically hypophysectomized as well. Our own long-term treated rats resumed growth when placed upon a stock diet, indicating that there was no permanent damage of the pituitary.

Although no deliveries were observed in any of the animals while on the thiourea ration, one was inseminated (Case 39) while on thiourea, and gave birth while on the normal food. Williams, et al.²⁷ have found no abnormalities on the gonads or other organs after thiouracil.

While it is true that the growth of the offspring may be retarded and its thyroid size and histologic activity increased by feeding 0.5 per cent thiourea to the mother, it is clear that no permanent damage has occurred. Although the experimental data gathered from the rodent have been in substantial agreement with those derived from the human being, the results would suggest caution in the employment of thiourea or thiouracil therapy in the treatment of pregnant hyperthyroid females.

Conclusions

1. A supplement of 0.5 per cent thiourea incorporated in the food fed to pregnant rats results in activation and hyperplasia of the thyroid gland, and retarded growth of the offspring.
2. The thiourea effect may be transmitted directly through the food, or indirectly through the placenta, or through the milk.
3. No births were observed in any of the rats while under treatment.
4. A return to a normal diet was marked by a return to normal growth and physiologic activity.
5. Caution in the use of thiourea or thiouracil therapy for cases of pregnancy complicated by hyperthyroidism is advised.

References

1. Astwood, E. B.: *J. A. M. A.* 122: 78, 1943.
2. Williams, R. H., and Bissell, G. W.: *New England J. Med.* 229: 97, 1943.
3. Himsworth, H. P.: *Lancet* 2: 465, 1943.
4. Rawson, R. W., Evans, R. D., Means, J. H., Peacock, W. C., Lerman, J., and Cortell, R. E.: *J. Clin. Endocrinol.* 4: 1, 1944.
5. Sloan, M. H., and Shorr, E.: *Science* 99: 305, 1944.
6. Paschkis, K. E., Cantarow, A., Rakoff, A. E., Walkling, A. A., Tourish, W. J.: *J. Clin. Endocrinol.* 4: 179, 1944.
7. McLaughlin, C. W., and McGoogan, L. S.: *AM. J. OBST. & GYNEC.* 45: 591, 1943.
8. Keston, A. S., Goldsmith, E. D., Gordon, A. S., and Charipper, H. A.: *J. Biol. Chem.* 152: 241, 1944.
9. Franklin, A. L., Lerner, S. R., and Chaikoff, I. L.: *Endocrinology* 34: 265, 1944.
10. Simpson, S.: *Quart. J. Exper. Physiol.* 6: 119, 1913.
11. Simpson, S.: *Quart. J. Exper. Physiol.* 14: 161, 1924.
12. Tatum, A. L.: *J. Exper. Med.* 17: 636, 1913.
13. Hammett, F. S.: *Am. J. Physiol.* 68: 1, 1924.
14. —: *Am. J. Physiol.* 76: 69, 1926.
15. —: *Endocrinology* 10: 29, 1926.
16. Salmon, T. N.: *Endocrinology* 23: 446, 1938.
17. —: *Endocrinology* 29: 291, 1941.
18. Scow, R. O.: *Anat. Rec.* 88: 456, 1944.
19. Goldsmith, E. D., Gordon, A. S., and Charipper, H. A.: *Federation Proc.* 3: 13, 1944.
20. Hughes, A. M.: *Endocrinology* 34: 69, 1944.
21. Mackenzie, C. G., and Mackenzie, J. B.: *Endocrinology* 32: 185, 1943.
22. Fugo, N. W., and Witschi, E.: *Acta Biologica Latvica* 8: 73, 1938.
23. Fugo, N. W.: *J. Exper. Zool.* 85: 271, 1940.
24. Kull, H. A.: *Anat. Rec.* 32: 133, 1926.
25. Ukita, T.: *Acta scholae med. univ. imp. in Kioto* 3: 287, 1919.
26. Williams, R. H., Kay, G. A., and Jandorf, B. J.: *J. Clin. Investigation* (In press).
27. Williams, R. H., Weinglass, A. R., Bissell, G. W., and Peters, J. B.: *Endocrinology* 34: 317, 1944.
28. Keston, A. S., Goldsmith, E. D., Gordon, A. S., and Charipper, H. A.: Unpublished observations.
29. Severinghaus, A. E.: *Cold Spring Harbor Symposia in Quart. Biol.* 10: 104, 1942.

SQUAMOUS METAPLASIA OF THE CERVIX UTERI

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THE occurrence of squamous epithelium in the cervical canal, which is normally lined by mucus-secreting columnar cells, has intrigued observers for more than 50 years. Added interest in this phenomenon has arisen during the past decades largely because of speculation on the possible relation to carcinoma of the cervix, particularly carcinoma in situ. A number of articles on this aspect of the subject and on differential diagnosis have appeared in the literature;¹⁻¹¹ the general impression left by these is one of emphasizing the benignancy of squamous metaplasia and deploring mistaken pathologic diagnosis of malignancy. Novak has tersely summed up this majority opinion in discussing a paper by Schmitz and Benjamin:³ "The so-called metaplasia is clearly benign and here again there is little reason to look on it as having any more influence on the development of cancer than pertains to any chronic irritative lesion." The erroneous diagnosis of malignancy in sections showing only exaggerated metaplasia has undoubtedly been made many times in the past, and conversely, the more grievous error of dismissing preinvasive carcinoma as simple metaplasia has also been committed, though less frequently. That the preinvasive cancers are malignant neoplasms in every sense has been shown by the excellent case studies and follow-up of Smith and Pemberton⁴ and Younge.⁵ This diagnostic error is declining in frequency as more attention is devoted to the character of the cells and as the old cardinal principle that cancers are necessarily invasive is abandoned.

Another aspect of the subject of squamous metaplasia of the cervix which has received considerable attention is the question of origin of the abnormal cells, and on this topic opinion is divided. The majority of observers seem to agree in whole, or in part, with Meyer¹⁰ who considers metaplasia a step in the healing of erosions. According to his hypothesis, squamous epithelium normally lines the lower portion of the cervical canal in the developing fetus. But as the mucus-secreting cells above begin to function, the squamous cells are destroyed by the macerating effect of the secretion to a line at or near the external os. Subsequently, the lower portion of the canal becomes a kind of battleground between columnar and squamous epitheliums, between the destructive effect of the mucous secretion from above, and the healing growth of squamous cells from below. Undoubtedly, such alternations do occur, but observations on our material suggest that such interplay is exceptional, and we are inclined to agree with Carmichael and Jeaffreson^{11, 12} that the atypical

epithelium arises in situ. Similarly, Wollner⁴ finds ectopic squamous epithelium only occasionally in extensive erosions where healing would logically be expected.

Meyer's explanation of isolated patches of squamous cells high in the cervical canal as being derived from groups of differentiated basal cells, which were segregated during the fetal adjustment period, is likewise questioned by Carmichael and Jeaffreson.¹¹ They contend that these basal cells are wholly undifferentiated and are capable of developing toward columnar or squamous epithelium. They find these cells in 95 per cent of human cervices and trace their maturation into fully-developed stratified squamous epithelium. The presence of mucinous material in cytoplasmic vacuoles of squamous-like cells in some involved areas suggests to them the dual potentialities of the basal-cell groups. In the end, the squamous epithelium may assume full adult characteristics, including glycogenation, so that the process is indeed a metaplasia. This line of reasoning is more in keeping with the earlier hypothesis of Ruge¹³ and others. Our own observations are confirmatory especially as regards the complete maturation of the metaplastic epithelium. Glycogenation has not been rare in our material, and we have seen an instance of keratinization of the ectopic squamous epithelium in a case of prolapse accompanied by cervical laceration and eversion.

The histologic appearance of the metaplastic epithelium has been fully described in the papers of Carmichael and Jeaffreson¹¹⁻¹² and has received much attention in this country from various authors. It is beyond our scope to reiterate these observations, but we would like to emphasize two points which we have found to be of value in differential diagnosis: First, the position and morphology of the cells which have been aptly described, especially as regards the outward displacement of the mucus-secreting columnar cells; second, the "festooning" effect which is achieved by the squamous cells in growing over the microscopic undulations of the endocervix. This latter especially pertains to the early phase.

Personal Study

To observe the incidence of squamous metaplasia and to attempt to find some etiologic factors, we have recorded data on a series of over 600 cervices studied for a period of the past four years. The cervices were fixed in toto, and sectioned serially around the external os at intervals of two to three millimeters. From four to ten or more blocks could be cut from each cervix, the number depending on the diameter and outline of the os. Two sections from each block were stained for study, one section being chosen from each face of the block, that is, one "shallow" and one "deep." In this manner, representative samples of the entire cervix were obtained. Blocks of the endometrium and upper levels of the cervical canal were also included with additional sections as indicated in the individual cases.

For convenience 100 consecutive cervixes, in which a maximum of satisfactory sections was obtained, were used for statistical analysis. Few significant differences between the figures for the entire series and this sample were noted, and the exceptions are mentioned here. The cervixes in sequence which were discarded as unsatisfactory were usually those traumatized incident to surgical removal. Data were recorded on the gross features (laceration, eversion), presence and degree of metaplasia (one to four-plus), location (surface and glandular), evidence of inflammation, and other disease. The clinical data were appended later from the hospital records and in some few cases are incomplete. The results are as follows:

Incidence: Squamous metaplasia was observed in 72 of the 100 cervixes in amounts varying from minimal (one-plus) to maximal (four-plus), the latter representing almost complete transformation of the columnar epithelium of the lower cervical canal. This figure is considerably higher than that reported by others. Carmichael and Jeaffreson¹² found an incidence of 41 per cent in their material and 14 of 75 cervixes showed metaplastic changes in a series by Schmitz, McJunkin and Macaluso.⁶ The percentage is somewhat higher in the studies of cervical polyps. Thus, while Fluhmann⁷ found metaplasia in only 59 of 1,195 specimens of cervix with an additional 33 instances of fully-mature squamous epithelium in cervical glands, he found metaplasia in 29 per cent of 100 polyps, and Mezer¹⁵ found it in 31 per cent of 1,636 polyps. The discrepancy between our figure and that of others may be due to differences in methods of examination and differences in interpretation. It was obvious in our material that minute areas of involvement could easily have been missed by anything less than routine serial blocking.

We have not observed a gross feature which would indicate the presence of metaplastic epithelium and have been unable to predict its presence from examination of the fresh specimen. In interpretation, we have freely pronounced as positive the minimal involvement often encountered, but we have not included the basal-cell groups or the occasional upward extension of stratified squamous epithelium from the pars vaginalis over a junctional ulcer.

Race: Race appears to have no effect on the incidence. Of 39 Negroes in the series, 30 or 77 per cent were positive, and of 61 whites, 42 or 69 per cent were positive.

Age: The youngest in the series was 21 and the oldest 51 years. The cases were divided by decades and the results tabulated. (Table I.) We feel that there is a significant increase in incidence from the third through the fifth decades and that this rise is emphasized by a correlated rise in severity. Carmichael and Jeaffreson¹² found an increase of from 35 per cent of cases under 50 years of age to 50 per cent of cases over 50 years, but considered the difference of little import. Our material in the age group over 50 years is insufficient, but the rising incidence by decades seems comparable.

Parity: We find no correlation between parity and the presence of metaplastic epithelium. Seventy-one per cent of the parous (1 to 10) subjects were positive. Of the nine nulliparas, eight or 89 per cent were positive. The one pregnant uterus included in the series was negative. Carmichael and Jeaffreson¹² likewise found no relationship between metaplasia and the number of births.

TABLE I

AGE GROUP	NUMBER	TOTAL METAPLASIA	PER CENT METAPLASIA	PER CENT POSITIVE			
				1-PLUS	2-PLUS	3-PLUS	4-PLUS
21 to 29	22	14	63.5	43.0	35.0	14.0	7.0
30 to 39	47	36	76.6	61.0	19.0	8.0	11.0
40 to 49	20	17	85.0	23.5	23.5	35.0	17.6
50+	5	3	60.0	66.0	33.0		

Menstrual History: This factor also was noncontributory. A wide variety of complaints of menstrual disorders was registered and no relation was evident for anyone. Of the seven women in or past the menopause, five of the cervixes (71 per cent) were positive.

Endometrial Phase: Our data for the series are incomplete. Of eight uteri having follicular (proliferative) endometria, seven or 87 per cent showed squamous metaplasia. Of nine uteri in the progestinal (secretory) phase, four or 44 per cent were positive. However, comparable data for another 100 cervixes with endometrial sections showed no appreciable deviation from the "normal" incidence in either phase.

Gross Features of Cervix: Gross appraisal of laceration and eversion was made on the fresh specimen and these were without effect as factors. Of the 58 cervixes showing frank tears with ectropion, 42 or 72 per cent were positive. Of those specimens presenting neither, 73 per cent showed metaplasia. This finding is contradictory to the expressed opinion of Meyer¹⁰ and his followers that metaplasia represents a step in the healing of "erosions," and is in keeping with the observations of Wollner⁴ as afore-mentioned.

Inflammation: We found it difficult to appraise this item and its possible relationship. Only a rare adult cervix is entirely free from evidence of inflammatory disease if the presence of subepithelial lymphocytes and plasma cells is a reliable criterion of inflammation. However, if the minimal cellular infiltrates be ignored and an arbitrary degree of reaction somewhat denser (two plus in our series) be used as the dividing line, there is suggestive but inconclusive correlation between chronic inflammation and the occurrence of metaplastic epithelium. Thus, the two were observed together in 30 instances, while inflammation without metaplasia was seen in nine cases. These latter include some instances of more acute disease, usually with ulceration, so that the number is probably disproportionately high. Metaplasia without inflammation was observed in 42 cases. Again it is questionable whether the figure is a true index, as there were individual instances in which complete differentiation of the metaplastic epithelium could be interpreted as healing with quiescence of any pre-existing inflammatory disease. Both inflammation and metaplasia were negative in 19 cases.

Other Disease: Under this grouping we have included the accompanying pelvic disorders other than cervical, and in most instances these were the chief clinical and pathological diagnoses. Fibromyomas constituted the most common cause for hysterectomy in the series and occurred in a total of 57 cases, alone in 37, and in combination with salpingitis in 20. Of these 57, 36 or 63 per cent were positive; the presence of salpingitis in combination or its absence was without effect, the figures being 81 per cent and 80 per cent positive, respectively.

The second most frequent complication was salpingitis alone, and six of eleven such cases (54 per cent) were positive. Malpositions of the uterus as a group showed no influence on the incidence (66 per cent

positive); but the three cases of frank prolapse were all positive. Carmichael and Jeaffreson¹² record an incidence of 46.5 per cent in 200 cervixes amputated for prolapse as compared with 33 per cent of 134 removed for other reasons.

A wide variety of disorders filled out the remaining cases. Endometriosis occurred three times and all were positive. Single instances of such diverse conditions as congenital malformation and adenocarcinoma of the fundus were included and the findings in the cervix were variable. The one pregnant uterus was negative.

Carcinoma in situ: Preinvasive carcinoma occurred twice in the series. This 2 per cent incidence of cancer is comparable to the figures given by Schiller¹⁶ (3 per cent in one series; 6 in 425 cases in another), but is somewhat lower than that of Wollner⁴ (2 cases in 59 cervixes). In both of our cases there was metaplasia in addition to the frank neoplasia, but the two processes were entirely distinct. The cancer cells treat the metaplastic epithelium with the same disrespect shown the normal columnar epithelium, uprooting and displacing it from beneath.

Discussion

The individual factors of those examined which appear to exert an influence on the development of metaplasia are age of the patient and inflammation or irritation of the cervix. Age of the patient per se is probably subordinate to age as a factor in ovarian function. The rising curve of incidence of squamous metaplasia from the third through the fifth decades of life roughly parallels the curve of declining ovarian activity with relative hyperestrinism; and from the data of Carmichael and Jeaffreson (our own material being insufficient), this curve appears to continue upward beyond 50 years. The experimental production of uterine metaplasia in various animals^{17, 18} by administering large doses of estrogens to castrates is presumptive evidence that a similar process pertains to metaplasia in the human cervix. Indeed, Wollner⁴ has described such a human case followed by biopsy while under estrone therapy. The uniform occurrence of metaplasia in the three cases of endometrial hyperplasia in this series lends some support, although admittedly the number is small. Speculation on hyperestrinism as a factor in the production of fibromyomas of the uterus is unwarranted here, but if, as has been suggested, such is possible, endocervical metaplasia in 81 per cent of 57 cases of fibromyomas in this series would be supportive. Against ovarian dysfunction as a factor is the nearly "normal" incidence observed in those individuals having adequate corpus luteum function as judged by the presence of secretory endometrium.

It is our opinion that chronic inflammation plays a more important part in the process than the figures indicate, although its mechanism as a local stimulus is vague. This opinion is based more on the notations of many individual sections than on the series as a whole. We not infrequently remarked on the close anatomic relationship between the two when only one or two of the sections of a given case were positive. It was not uncommon to find isolated patches of metaplastic squamous epitheli-

um accompanied by local round-cell infiltration while the surrounding areas were almost entirely free of both. In the more diffusely involved cervixes, the association is not so readily apparent. Nor is association common in the more acutely inflamed lesions, but these are often devoid of all epithelium. In our material, the presence of metaplasia in chronic inflammatory disease seems removed from any function in the healing of erosions, as the ratio in everted and noneverted cervixes is almost exact (72 per cent and 73 per cent), and eight of nine nulliparous cervixes, grossly free from any lesion, showed varying degrees of metaplasia in the endocervix. Circumferential involvement of the endocervix just proximal to the external os was a fairly frequent observation in nulliparous specimens and in parous specimens in which near perfect healing produced some degree of stenosis. The dilated canal immediately above was usually filled with thick mucus, sometimes inspissated, suggesting that the secretion itself, in the absence of frank infection, may be sufficient stimulus to induce basal-cell proliferation and squamous metaplasia.

Whatever the etiology and significance of the metaplastic epithelium, it seems to bear no relation to malignant disease except for a possible common ancestral cell. We have seen nothing to suggest direct conversion of metaplastic to neoplastic cells. But a common forbear of these otherwise divergent processes does seem a distinct possibility, as has been suggested before.⁴ We point out the locus common to both, beginning within the cervical canal and not on the pars vaginalis and the oblique tapering against the normal stratified squamous epithelium at occasional points only in the early stages. In both instances of carcinoma in this series, the neoplasms were removed from the pars vaginalis and occupied positions comparable to the usual location of metaplastic epithelium. Neither involved the whole circumference of the endocervix, nor the whole extent of the surface in any section. The tendency of the cancer cells to grow along natural surfaces, displacing the pre-existing epithelium, whether columnar or squamous, and to remain in situ for some time suggests a kinship to the metaplastic cells.

References

1. Novak, E.: The Pathologic Diagnosis of Early Cervical and Corporeal Cancer With Special Reference to the Differentiation From Pseudo-Malignant Inflammatory Lesions, *AM. J. OBST. & GYNEC.* 18: 449-471, 1929.
2. TeLinde, R. W.: Cancer-like Lesions of the Uterine Cervix, *J. A. M. A.* 101: 1211-1217, 1933.
3. Schmitz, H., and Benjamin, E. L.: Early Histologic Diagnosis of Carcinoma of the Uterine Cervix, *J. A. M. A.* 103: 808-810, 1934.
4. Wollner, A.: The Early Diagnosis of Cervical Carcinoma, *Surg., Gynec. & Obst.* 68: 147-154, 1939.
5. Broders, A. C.: Carcinoma in Situ Contrasted With Benign Penetrating Epithelium, *J. A. M. A.* 99: 1670-1673, 1932.
6. Schmitz, H., McJunkin, F. A., and Macaluso, M. A.: Histopathology of Epithelial Hyperplasia and Neoplasia of the Cervix Uteri, *AM. J. OBST. & GYNEC.* 27: 336-341, 1934.
7. Fluhmann, C. F.: Epidermization of the Cervix Uteri and Its Relation to Malignancy, *AM. J. OBST. & GYNEC.* 15: 1-16, 1928.

8. Smith, G. van S., and Pemberton, F. A.: The Picture of Very Early Carcinoma of the Uterine Cervix, Surg., Gynec. & Obst. 59: 1-8, 1934.
9. Younge, P. A.: Preinvasive Carcinoma of Cervix, Arch. Path. 27: 804-807, 1939.
10. Meyer, R.: Die Epithelentwicklung der Cervix und Portio vaginalis Uteri und die Pseudoerosio congenita, Arch. f. Gynäk. 91: 579-598, 1910.
11. Carmichael, R., and Jeaffreson, B. L.: Basal Cells in the Epithelium of the Human Cervical Canal, J. Path. & Bact. 49: 63-68, 1939.
12. Carmichael, R., and Jeaffreson, B. L.: Squamous Metaplasia of the Columnar Epithelium in the Human Cervix, J. Path. & Bact. 52: 173-186, 1941.
13. Ruge, C.: Ztschr. f. Geburtsh. u. Gynäk. 67: 533, 1910. Quoted by Carmichael and Jeaffreson and others.
14. Novak, E.: Pseudomalignant and Precancerous Lesions of the Cervix, J. A. M. A. 108: 1145-1151, 1937.
15. Mezer, Jacob: Metaplasia and Carcinoma in Cervical Polyps, Surg., Gynec. & Obst. 75: 239-244, 1942.
16. Schiller, W.: Early Diagnosis of Carcinoma of Cervix, Surg., Gynec. & Obst. 56: 210-222, 1933.
17. McEuen, C. S.: Metaplasia of Uterine Epithelium Produced in Rats by Prolonged Administration of Oestrin, Am. J. Cancer 27: 91-94, 1936.
18. Korenchevsky, V., and Hall, K.: The Bisexual and Cooperative Properties of the Sex Hormones as Shown by the Histologic Investigation of the Sex Organs of Female Rats Treated With These Hormones, J. Path. & Bact. 45: 681-708, 1937.

THE RAPID TREATMENT OF EARLY SYPHILIS DURING PREGNANCY

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THE treatment of the prenatal patient with early infectious syphilis has always been a problem. The patient frequently presents herself for the first time so late in pregnancy that it is difficult to give her sufficient treatment. Minor reactions create sufficient inconvenience that the patient fails to receive treatment regularly, while severe reactions necessitate at least a temporary interruption of vital therapy so necessary if the transmission of the disease to the unborn child is to be prevented.

At Bellevue Hospital in December, 1939,¹ we adopted massive arsenotherapy for patients with early infectious syphilis and in 1940, it was decided to give the same type of treatment to prenatal patients with early syphilis. It was felt that intensive therapy would have the advantage of so favorably affecting the patient with early syphilis prior to the fourth month of gestation, that she would not transmit the disease. On the other hand, such therapy given to the infected mother who is further advanced with her pregnancy may appreciably effect a syphilitic infection already transmitted to her offspring.

In 1933, Chargin, Leifer and Hyman successfully shortened the treatment of early syphilis to a period of five days by continuous intravenous drip administrations of neosalvarsan for ten hours daily. Later experiments proved that mapharsen was a much less toxic drug for massive therapy. At Bellevue Hospital, we adopted the rapid massive treatment without using the intravenous drip. The total dosage of mapharsen prescribed was subdivided into equal doses which were given intravenously by syringe at regular intervals for a six- to ten-day period. Since it was found that the administration of more than 1 Gm. of mapharsen in this period was associated with encephalopathy in over one per cent of all patients treated, the total dosage of mapharsen was reduced. Unfortunately, relapses were found to be more frequent in patients who received less than 0.9 Gm. It was then decided to use fever to re-enforce the action of these lowered doses of mapharsen. Various combinations of mapharsen with fever induced by typhoid vaccine were used in order to find a safe and effective plan of treatment.

In these schedules, two injections of about 0.06 Gm. of mapharsen were used on at least one day of treatment.² After much experimentation, it was finally decided that the maximum dose of mapharsen given should be approximately 1 mg. per kilogram of body weight, and that only one injection was to be given a day.³ The average patient would then receive ten daily injections of about 0.06 Gm. of mapharsen. To re-enforce the treatment of this low dosage, four fevers induced by typhoid vaccine were included in the ten days. The fevers were given on the second, fourth, sixth and eighth days. The first fever was induced with an initial injection of 0.1 c.c. triple typhoid vaccine intravenously; the second with 0.2 c.c.; the third with 0.4 c.c., and the last with 0.6 cubic centimeters. From two to three hours after the initial injection, another dose of equal amount was given in most cases. In general, a fever of at least 104° F. for about four hours was obtained. In June, 1943, we added bismuth to our schedule of rapid treatment, giving 0.1 Gm. of bismuth salicylate in oil on the first, third, seventh and tenth days of therapy. Thus, our standard plan of therapy came to be as follows:

TREATMENT	DAYS									
	1	2	3	4	5	6	7	8	9	10
Mapharsen—1 mg. per kilogram	x	x	x	x	x	x	x	x	x	x
Bismuth salicylate in oil—100 mg.	x		x				x			x
Typhoid vaccine in c.c.		0.1		0.2		0.4		0.6		
		0.1		0.2		0.4		0.6		

Choice and Preparation of Patients

The plan of therapy for the treatment of syphilis in the nonpregnant acted as a proving ground before carrying out a similar procedure in the pregnant patient. With a few exceptions, cases with early syphilis were chosen first since the obvious effects of therapy could be more readily appraised in these cases. Thus, there were 36 pregnant patients with early infectious syphilis: two with seronegative primary syphilis, three with seropositive primary syphilis, 28 with secondary syphilis and three with relapsing secondary syphilis. In this group the syphilitic lesions appeared in 16 during the first trimester, in 13 during the second, and in seven during the last trimester. In addition, five patients with early latent syphilis and two with late latent syphilis were treated. Intensive treatment was given anytime during the course of pregnancy depending upon the time the patient presented herself. Contraindications to such intensive therapy include active tuberculosis, nephritis, decompensated heart disease, toxemias of pregnancy and any chronic hepatic disease. No such contraindications were present in any of this group.

All patients were subjected to a complete physical examination to rule out any medical or obstetrical contraindication to intensive therapy. Blood pressure, urine examinations and blood counts were taken before treatment was started and frequently throughout the course of therapy. Cisternal punctures were performed on about half of the cases with no resulting harmful effects.

Reactions to Intensive Therapy in General

In the nonpregnant patients, encephalopathy was practically the only severe reaction occurring with intensive therapy. Among 321 treatment courses with mapharsen alone, in a six- to ten-day period, the incidence of encephalopathy was 1.6 per cent.³ In a subsequent series of 588 treatment courses with combined fever and mapharsen where two injections of about 0.06 Gm. of mapharsen were given on at least one day of treatment, the incidence of encephalopathy was 1.36 per cent.³ In the total series of 909 treatment courses, the mortality rate from encephalorrhagia was one in 300, a mortality rate much too high to justify this plan of therapy. With the subsequently employed ten-day plan of treatment previously outlined, 1,303 treatment courses were given, the incidence of encephalopathy being 0.3 per cent with a mortality rate of 1 in 1,303. In the total group of 2,212 patients treated, several other reactions were noted. One patient developed a mild arsenical dermatitis. There were 100 instances of early acute arsenical erythemas and urticarias. In addition, mild transient jaundice occurred in five patients, in three during hospitalization, in 1 three weeks, and in 1 six months after therapy. There were four instances of transient hematuria noted in those patients receiving mapharsen and fever therapy. Also, one patient developed agranulocytosis and recovered completely. Mild peripheral neuritis was noted in five instances. Nausea and vomiting occurred with great frequency following the first few injections of mapharsen. In very few instances did this persist with subsequent injections, and never did this reaction warrant discontinuation of therapy. Concomitantly with fever, practically all patients complained of headache and malaise. When these latter symptoms are severe they may be relieved by sedatives, the choice being morphine.

Types of Treatment and Reactions With Intensive Therapy During Pregnancy

Forty-three pregnant patients were treated. Six cases of secondary syphilis were treated with mapharsen alone: one patient received 1.2 Gm. mapharsen in six days, one received 0.88 Gm. in nine days, three 0.84 Gm. in six days, and one patient 0.72 Gm. in six days, depending upon the dosage in vogue at the time. Eight patients received from 0.6 to 0.8 Gm. of mapharsen and two to three fevers in seven to eight days. Twenty-nine patients were placed on the ten-day plan of treatment finally adopted with 0.5 to 0.6 Gm. of mapharsen and three to four fevers in the ten-day period. Twenty-three of these patients also received bismuth.

In this pregnant group, vomiting frequently followed the first few injections of mapharsen. In only one instance did a patient continue vomiting throughout the entire course of mapharsen therapy. With fever induced by typhoid vaccine, subcutaneous injections of morphine sulfate were given to the pregnant patients who complained of vomiting, headaches, generalized aches and pains with marked relief. One patient had a ninth day erythema of Milian. In three patients nose bleeds were encountered. There were no instances of jaundice, agranulocytosis, or peripheral neuritis. Unfortunately, the last patient treated developed arsenical encephalopathy and died following the fifth injection of 0.07 Gm. of mapharsen with one previous fever episode. (This is the single fatality noted in the total 1,303 courses of treatment previously mentioned.)

Three patients complained of mild abdominal cramps during their first episode of fever. These abdominal cramps were not associated with obvious uterine contractions. One of these three patients as well as another who was free from abdominal pain, had a slight bloody vaginal discharge on the day following fever therapy. This discharge lasted for a few hours and then subsided. Further mapharsen therapy as well as typhoid vaccine was continued without a recurrence. One patient who was admitted with early syphilis, vaginal bleeding and abdominal cramps withstood mapharsen and fever therapy without any recurrence of bleeding or abdominal pain.

Twenty-six of the 29 patients who were placed on the ten-day plan of therapy completed this treatment. Of the three patients who did not complete their course of treatment, one was the patient who died of arsenical encephalopathy; one was a patient with secondary syphilis who was four and one-half months pregnant, and delivered a stillborn fetus on the second day of treatment having had two injections of mapharsen and one fever; the third was a patient with late latent syphilis who was six months pregnant, and delivered a stillborn fetus after 0.42 Gm. of mapharsen and three fevers. The last patient gave a history of having had six spontaneous abortions, several before and several after she had acquired syphilis.

Results of Treatment of Pregnant Patients With Early Infectious Syphilis

The results of treatment in the mothers and babies are classified according to the type of intensive therapy given, i.e., mapharsen alone, the seven- to eight-day plan of treatment with mapharsen and fever, and the finally adopted ten-day plan with mapharsen, bismuth and fever.

Six patients with secondary syphilis were treated with mapharsen alone. (Table.) Two patients who were treated in the second trimester relapsed shortly before delivery with the result that one patient (V. M.) delivered a premature macerated stillbirth, and the other (J. S.) a full-term baby who developed secondary syphilis two weeks after birth. The other four patients delivered babies who were apparently free from syphilis. One of these children was seropositive at birth and had negative serologic tests for syphilis (hereafter abbreviated as STS) at three, six and nine months of age. One baby was not examined at birth but had negative STS at five months of age. The other two were seronegative at birth; one having negative STS at eight months of age and the other lost to subsequent follow-up. Of the mothers who delivered, the four apparently healthy babies, one had negative STS and 3 positive STS at the time of delivery.

In the second group (Table II), eight patients with primary, secondary or relapsing secondary syphilis received 0.6 to 0.8 Gm. of mapharsen and two to three fevers induced by typhoid vaccine. One patient (A. B.) at thirty-seven weeks delivered a macerated fetus; the mother's STS was positive at the time of delivery. The other seven patients delivered apparently healthy babies, six at term and one close to term. The seventh day STS were negative in six of the babies and positive in one of the babies. The last baby had positive STS two and one-half months after birth, but completely negative STS, three, four and seven months after birth. Two have not been seen since birth, and the other four had negative STS when examined at three to twenty-four months of age. In

TABLE I. THERAPEUTIC RESULTS IN PATIENTS TREATED WITH MAPHARSEN ONLY

PATIENT	LENGTH OF PREGNANCY AT ONSET OF TREATMENT	MOTHER'S INTRA-PARTUM STS*	TERM OR PREMATURE	BABY'S CONDITION	BABY'S 7TH DAY STS	FOLLOW-UP STS OF BABY	FOLLOW-UP OF MOTHER
V. M.	5 months	Strongly positive	32 weeks	Macerated	--	--	Relapsed before delivery.
J. S.	6 months	Strongly positive	Term	Good	Positive	Secondary syphilis 2 weeks after delivery	Relapsed before delivery.
M. C.	5½ months	Negative	Term	Good	Negative	Negative at 1 and 8 months	Negative 18 months after treatment. Spinal fluid normal.
E. T.	4½ months	Strongly positive	28 weeks	Good	No report	Negative at 5 months	Positive 4 years after treatment. Spinal fluid normal.
E. N.	8 months	Strongly positive	Term	Good	Positive	Positive 1 month; negative 3, 6 and at 9 months	Negative 27 months after treatment. Spinal fluid normal.
C. N.	7½ months	Positive	Term	Good	Negative	Lost	Lost.

*STS = serologic tests for syphilis.

TABLE II. THERAPEUTIC RESULTS IN PATIENTS TREATED IN 7 TO 8 DAYS WITH 0.6 TO 0.8 GM. OF MAPHARSEN AND 2 TO 3 FEVERS INDUCED BY TYPHOID VACCINE

PATIENT	LENGTH OF PREGNANCY AT ONSET OF TREATMENT	MOTHER'S INTRA-PARTUM STS*	TERM OR PREMATURE	BABY'S CONDITION AT BIRTH	BABY'S 7TH DAY STS	FOLLOW-UP STS OF BABY	FOLLOW-UP OF MOTHER
A. B.	4½ months	Positive	37 weeks	Macerated	--	--	Lost.
L. W.	3½ months	Positive	Term	Good	Negative	Negative at 6 weeks and at 6 months	Negative 23 months after treatment. Spinal fluid normal.
E. M.	8½ months	Strongly positive	Term	Good	Negative	Negative at 3 months	Negative 5 months after treatment.
D. D.	6½ months	Positive	Term	Good	Negative	Negative at 2 and 5 months	Negative 9 months after treatment.
A. C.	5 weeks	Negative	36 weeks	Good	Negative	Negative at 3 and 24 months	Negative 30 months after treatment. Spinal fluid normal.
M. B.	2 months	Negative	Term	Good	Negative	Lost	Lost.
E. S.	4½ months	Negative	Term	Good	Negative	Lost	Negative 11 months after treatment.
M. L.	8 months	Strongly positive	Term	Good	Positive	Positive at 1 and 2½ months. Negative at 3, 4 and 7 months	Negative 15 months after treatment. Spinal fluid normal.

*STS = serologic tests for syphilis.

TABLE III. THERAPEUTIC RESULTS IN PATIENTS TREATED IN 10 DAYS WITH 0.6 GM. MAPIARSEN AND FOUR FEVERS INDUCED BY TYPHOID VACCINE

PATIENT	LENGTH OF PREGNANCY AT ONSET OF TREATMENT	MOTHER'S INTRA-PARTUM STS*	TERM OR PREMATURE	BABY'S CONDITION AT BIRTH	BABY'S 7TH DAY STS	FOLLOW-UP STS OF BABY	FOLLOW-UP OF MOTHER
L. N.	2 months	Positive	16 weeks	4 mo. fetus	--	--	Negative 10 months after treatment.
F. B.	3 months	Positive	29 weeks	Good	Positive	Died 6 days after birth	Positive 6 months after treatment. Spinal fluid normal.
M. B.	6 months	Positive	Term	Good	Positive	Too early	Too early.
R. W.	8½ months	Positive	Term	Good	Positive	Too early	Too early.
L. W.	6 months	Positive	Term	Good	Positive	Negative at 3 months	Negative at 3 months.
R. W.	3 months	Negative	Term	Good	Negative	Negative at 5 months	Negative 14 months after treatment.
R. E.	7 months	Positive	Term	Good	Negative	Negative at 2, 4, 7 and 12 months	Negative 12 months after treatment. Spinal fluid normal.
F. S.	4 months	Positive	32 weeks	Good	Negative	Negative at 2 months	Negative at 11 months. Spinal fluid normal.
R. W.	2 months	Negative	Term	Good	Negative	Negative at 1 month	Negative 7 months after treatment.
E. D.	6 months	Negative	Term	Good	Negative	Negative at 4 months	Negative 5 months after treatment.
T. J.	4½ months	Negative	Term	Good	Negative	Lost	Negative 6 months after treatment.
A. O.	2 weeks	Negative	Term	Good	Negative	Lost	Negative 9 months after treatment.
J. S.	2½ months	Negative	Term	Good	Negative	Lost	Negative 7 months after treatment.
R. L.	3 months	Negative	Term	Good	Negative	Lost	Negative 4 months after treatment.
R. H.	2 months	Negative	Term	Good	Negative	Too early	Negative 7 months after treatment.
N. C.	7 months	Positive	Term	Good	Negative	Lost	Positive 2 months after treatment.

*STS = serologic tests for syphilis.

summary, of the eight babies delivered, there were seven apparently healthy babies and one premature macerated stillbirth. Of the mothers who delivered the apparently healthy babies, three were seronegative, and four were seropositive at the time of delivery.

In the third group, 21 patients with early infectious syphilis were placed on the finally adopted ten-day plan of therapy. Of these, three have been lost from observation, and two have not delivered as yet. Therefore, the discussion of the results of this group is confined to 16 patients (Table III). One patient (L.N.) had a spontaneous abortion in the fourth month of pregnancy, two months after completion of treatment. Although her STS were positive at the time of abortion, she received no further treatment and eight months later her STS became negative. One premature baby (F.B.) of twenty-nine weeks' gestation who was seropositive at birth, died six days after delivery. The other 14 patients delivered apparently healthy babies, one premature and 13 at term. Three of these babies were seropositive and 11 seronegative at birth. Two of the seropositive babies were delivered so recently that further STS have not been done as yet. The third baby who was seropositive at birth, now has negative STS at three months of age. Of the 11 babies who were seronegative at birth, five were followed and were negative at one to twelve months of age, while six have not had STS since birth. In summary, of the 16 babies delivered, there were 14 live infants, 12 of whom have negative serologic tests, and two with seropositive tests at birth who have not been rechecked. There were two failures. Of the 14 mothers who delivered live infants, six were seropositive and eight seronegative at the time of delivery.

Analysis of Results

Combining the results of the three plans of therapy we find that of the 30 babies delivered, 23 have seronegative reactions, 14 having been followed one to twenty-four months. Seven have been classified as failures; the two premature macerated fetuses, the four-month stillborn fetus, the premature child who died 6 days after birth, the child who developed secondary syphilis, and the two recently born children who were seropositive at birth and have not been rechecked. The last two while included among the failures may subsequently prove to have negative STS as did three other babies, who while seropositive at birth, became seronegative at three months of age. The mother who aborted the four-month fetus was seronegative eight months later, and it is very possible that the abortion was not due to her syphilitic infection.

Since it is admittedly infrequent for a child born with negative STS to develop a positive reaction at a later date, the nine children seronegative at birth but subsequently lost to follow-up have been included among the probable good results with the 14 who were followed for longer periods. The probable good results (23 out of 30) would then be at least 76.6 per cent.

Relationship of the Onset of Treatment to the Length of Gestation

In the routine treatment of syphilis in pregnancy, a direct relationship can be observed in the results obtained and the time in pregnancy that treatment was started.⁴ No such relationship is apparent in the intensively treated cases. Of the nine mothers who were treated in the first trimester of pregnancy, seven babies have been classified as good

results, and of the 13 who were treated in the second trimester, nine delivered babies free from syphilis. Eight mothers were treated in the third trimester and seven of their babies were healthy.

Intensive Treatment of Latent Syphilis During Pregnancy

While no effort was made to obtain a series of intensively treated latent syphilitic prenatal patients, seven pregnant women with latent syphilis were given this type of therapy because it was felt that they were too unreliable for the orthodox plan of treatment. Of these seven, three had syphilis of less than six months' duration. One of these was the girl who died from arsenical encephalopathy, one has been lost from observation and one has not delivered as yet. Four patients had syphilis of unknown duration. Of these, two had babies with negative STS at birth and two months after birth. One who was six months pregnant delivered a stillborn fetus in the middle of her treatment, and one patient has not delivered as yet. Obviously, no conclusion can be drawn from this small series of cases.

Results of Therapy in Patients Who Became Pregnant After Previously Receiving Intensive Therapy for Early Syphilis

Most authorities agree that all pregnant women who have or have had syphilis should be treated with each pregnancy irrespective of previous therapy, or the status of their serologic tests. We wished to learn whether it was necessary to treat patients who had received massive arsenotherapy prior to pregnancy.

After a patient finished the rapid treatment, no further therapy was given unless a relapse occurred. Thirty-two of our intensively treated patients subsequently became pregnant and received no further treatment during their pregnancy. Two had previously been treated for early latent syphilis, and 30 for secondary syphilis. Of these 32 patients, 27 delivered healthy babies, 26 at term and one after 30 weeks of gestation. Five had spontaneous abortions of which only one was due to syphilis. Of the twenty-seven who had healthy babies, four delivered ten to eleven months after antisyphilitic treatment, eight delivered twelve to seventeen months, five delivered eighteen to twenty-three months, and 10 delivered twenty-four months after their intensive therapy. Twenty-five mothers had negative intrapartum serologic tests for syphilis. All of these had seronegative babies. Two mothers had positive intrapartum serologic tests for syphilis; one baby was seronegative at birth and one was seropositive, but became seronegative within one month. Three of these patients became pregnant a second time subsequent to previous intensive treatment and these babies had negative serologic tests for syphilis.

In this group of previously intensively treated patients, five patients had spontaneous abortions. One became pregnant three months after treatment. At the onset of her pregnancy her serologic tests for syphilis were slightly positive. She aborted at the end of three months at which time her STS were negative. She has been followed for forty-seven months since then, and has had negative STS as well as a normal spinal fluid. Another patient had negative STS four months after treatment. She became pregnant one year after treatment and aborted after two months. For three months following the abortion, she has had consistently negative STS and normal spinal fluid findings. A third patient became pregnant two months after completion of treatment and

aborted at the end of three months. Her STS were slightly positive at the time of her abortion, but became completely negative during the next two months. A fourth patient who had negative STS at the onset of her pregnancy four months after previous intensive treatment subsequently delivered a six-month fetus which died one hour after birth. The mother was followed for twenty-seven months during which time she had negative STS and normal spinal fluid findings. A fifth patient who conceived soon after completing her intensive therapy delivered a six-month macerated fetus at another hospital. She was seen by us one month later, at which time she had secondary syphilis with dark-field positive lesions.

Thus, of the 32 patients, five aborted and 27 had normal babies one being premature. In only one instance of the five early terminations can syphilis be held responsible.

Comparison of Therapeutic Results and Reactions of Massive Arsenotherapy With Routine Treatment

Prior to the advent of intensive therapy, the records of the prenatal syphilis clinic at Bellevue Hospital, since 1936, reveal that 34 patients with early infectious syphilis received routine treatment during their pregnancy. Of these 34, one died from arsenical encephalopathy and one was lost from observation. Of the remaining 32 patients, five delivered macerated stillbirths and 11 delivered syphilitic live babies, two of whom died a few weeks after birth while under therapy. Sixteen babies were apparently free from syphilis, having negative STS from seven days to two years after birth. The probable satisfactory results under this plan of therapy are 50 per cent as compared to the minimum of 76.6 per cent obtained by massive arsenotherapy. The poor results of the routine type of therapy are due to the inadequate, irregular treatment received by these patients. The inadequacy of treatment is due to the limited time available with routine treatment to give the patient a sufficient amount of the arsenical drugs. Only four received more than ten injections of arsenical drugs before the termination of pregnancy. Among 23 prenatal patients with early infectious syphilis who received no antisyphilitic therapy, no baby escaped syphilis. As a result of the superiority of intensive therapy as compared to routine therapy, there is a diminishing incidence of prematurity and maceration as well as live syphilitic babies. Table IV shows the comparative results in the three groups.

TABLE IV. COMPARISON OF RESULTS OF TREATMENT OF PREGNANT PATIENTS WITH EARLY INFECTIOUS SYPHILIS

TYPE OF TREATMENT	TOTAL NUMBER FOL- LOWED	PREMA- TURE	MACER- ATED	NUMBER OF NEONATAL DEATHS DUE TO SYPHILIS	LIVE SYPHILITIC BABIES UN- DER TREAT- MENT	BABIES AP- ARENTLY FREE FROM SYPHILIS
Massive arsenotherapy	30	7*	2	1	1	23 (76.6%)
Routine treatment	32	10†	5	2	9	16 (50%)
No treatment	23	14	6	5	12	0 (0%)

*Two of these premature babies were free from syphilis.

†Three of these premature babies were free from syphilis.

Of the 34 patients given routine treatment for early infectious syphilis, three were treated with mapharsen, 8 with arsphenamine and 23

with neoarsphenamine. A study of the reactions encountered in this group revealed one death due to arsenical encephalopathy after two injections of neoarsphenamine (0.2 and 0.3 Gm.), five cases of jaundice (four from neoarsphenamine), and one case of exfoliative dermatitis after neoarsphenamine. In the group of 43 prenatal patients who received massive mapharsen therapy, one death occurred from arsenical encephalopathy, the onset of this complication developing after the fifth mapharsen injection, and there were no cases of jaundice or exfoliative dermatitis.

Discussion

From the data given, the rapid treatment of early syphilis in pregnant women has given encouraging results. In a group of 30 prenatal patients with early infectious syphilis who completed treatment, we have classified seven as failures. However, not all of these babies are definitely syphilitic. Two babies who were seropositive at birth had been delivered too recently for re-examination. These babies at a later date may prove to be seronegative. In the case of the four-month stillborn fetus, the mother became seronegative subsequently without further treatment. No autopsy was obtained in this case. It is extremely unlikely for syphilis to produce abortion prior to the fourth month of gestation and therefore, it is questionable whether this poor result was due to a syphilitic infection. In view of the uncertain status of these three cases, if they were to be deducted from the series, there remains four poor results ascribable to syphilis out of a total of 27 cases, a corrected salvage rate of 85 per cent. Based upon the same assumptions, the results with the various plans of rapid therapy are as follows: Of the six patients treated with mapharsen alone, probable good results were obtained in four (66 per cent); of eight patients treated with the seven-day plan of combined mapharsen and fever therapy, there were seven good results (87 per cent); of the 13 patients treated with the ten-day plan of combined mapharsen, bismuth and fever, there were 12 good results (92 per cent).

More severe reactions were encountered in the prenatal patients with the routine plan of therapy than were found with the intensive plan of therapy. However, the routine plan of treatment consisted chiefly of the administration of arsphenamine and neoarsphenamine. Admittedly, the reactions with these drugs are greater than with mapharsen. It is well established that pregnant women have an increased susceptibility to arsenical drugs with resulting reactions particularly encephalopathy. One death from this cause resulted after only five injections of mapharsen in the rapid plan of treatment, and one death occurred from 2 small doses of neoarsphenamine in the routine plan of therapy. This emphasizes the need for caution in the use of arsenical drugs when treating syphilis in pregnancy. It must be recognized, however, that from the foregoing data massive mapharsen therapy combined with fever and bismuth has proved less toxic than the older forms of routine therapy.

Conclusions

1. Forty-three pregnant patients were treated for syphilis with massive mapharsen therapy. One death from arsenical encephalopathy occurred in this group. Of the 30 patients with early infectious syphilis who completed treatment and were kept under observation, good results from this therapy were obtained in a minimum of 76.6 per cent. If the babies not proved to be syphilitic are eliminated from the calculations, the probable good results would be 85 per cent.

2. At the Bellevue Hospital prenatal syphilis clinic between 1936 to 1940, prior to the advent of massive arsenotherapy, there were 34 pregnant patients treated for early infectious syphilis with routine therapy. One death occurred from arsenical encephalopathy, five patients developed jaundice and one exfoliative dermatitis. Only 50 per cent of the offspring were free from syphilis.

3. In the relatively small series reported here, intensive therapy proved safer and more effective than routine treatment. Nevertheless, there remains the risk of arsenical encephalopathy and this is probably greater with intensive mapharsen therapy than when the same drug is employed in routine treatment.

4. Massive mapharsen therapy in the treatment of early infectious syphilis prior to the onset of pregnancy has yielded excellent results, since there was only one failure among 32 patients so treated. This failure occurred in a mother who had a cutaneous relapse.

References

1. Thomas, E. W., and Wexler, G.: Rapid Treatment of Early Syphilis With Multiple Injections of Mapharsen, *Am. J. Pub. Health* 31: 545, 1941.
2. Thomas, E. W., and Wexler, G.: Rapid Treatment of Early Syphilis, *Arch. Dermat. & Syph.* 47: 553, 1943.
3. Thomas, E. W., and Wexler, G.: Review of 2,144 Courses of Rapid Treatment for Early Syphilis, *Am. J. Syph., Gonorr. & Ven. Dis.* 28: 529, 1944.
4. Speiser, M. D.: Syphilis in the Pregnant Woman, *New York State J. Med.* 41: 240, 1941.

NEISSERIAN INFECTION IN PREGNANCY*

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Introduction

AN EARLIER and confusing experience with smear and culture in the diagnosis and management of gonorrheal infection complicating pregnancy prompted the present study. The first observation was confined to antepartum patients in a Prenatal Clinic for expectant mothers of low income, who had relatively good social standards. A medical technician trained in the interpretation of smear and cultural procedures, the necessary laboratory facilities, and an experienced venereal disease contact investigator were accessible. From the beginning, it was apparent that certain patients had repeated positive smears, negative cultures, and sexual partners with no evidence of infection as shown by negative smears, cultures, and clinical findings. It was likewise noted that patients with positive cultures, usually had positive smears, clinical evidence of infection, and their contacts had gonorrhea. These disconcerting findings caused suspicion as to the effectiveness of smear alone in the diagnosis of gonorrhea, and increased the responsibility of making a correct disposition of the cases. It appeared unjust to stigmatize the expectant mother with a diagnosis of gonorrhea and subject her to the marital discord which resulted when she informed her husband that she was not only pregnant but had gonorrhea, when neither had little if any evidence of infection. The problem was further magnified by the seemingly unnecessary cost of treatment and delivery, when the hospital isolation rules required a private room and special nurses for both mother and infant, if smear from the urethra of mother or eyes of infant was positive.

This study was planned in an attempt to clarify some of the problems encountered in the antepartum patients, namely: How efficient is smear compared to culture in the diagnosis of gonorrhea? Can the gonococcus be transmitted from the antepartum to the postpartum state and if so how? Is it activated by the trauma of labor, and if so can it be found in the intrapartum and postpartum discharges from the vagina? When is the patient free of gonococci following treatment? How frequently is the gonococcus the cause of postpartum morbidity? Is the diagnosis more confusing in the pregnant than in the nonpregnant patient?

*Thesis submitted to the faculty of the Graduate School of Medicine of the University of Pennsylvania, toward the requirements of the degree of Master of Medical Science (M. Sc. [Med.]) for graduate work in obstetrics and gynecology.

Theory

Whereas, the first observation was confined to the antepartum period, this study was extended into the intrapartum and postpartum periods. It was predicated on the belief that chronic gonorrheal infection localizes in the deep urethral tissues, adjacent glands and ducts, Bartholin glands and ducts, and in the cervical glands;¹ and that the gonococcus may be pressed out of the deep cervical glands,² and expelled in the mucous plug which may contain a large part of the proliferated cervical mucosa,^{2, 3} and may be activated by the traumatizing effect of labor,² and found later in the show and lochia and recovered by culture. It is recognized that trauma of instrumentation materially exaggerates a latent infection, and the passage of an instrument into the urethra to stir up a latent focus of infection is considered most useful⁴ by the male urologist. Therefore, one might expect a higher incidence of morbidity, with clinical evidence of disease and gonococci in the discharges of parturient patients harboring gonorrheal infection, whose glandular structures have experienced such a marked degree of trauma.

Method

Urethral and cervical smears and cultures were taken on all patients admitted to the Prenatal Clinic. Urethral smears were taken on all patients admitted to the hospital in labor and checked with culture if positive, suspicious, or patient had clinical evidence of infection. The smear and culture were taken at the same time in as many patients as possible. A specimen of show was taken at or near complete cervical dilatation, and urethral and lochial cultures were taken on about the first, third, fifth, and seventh postpartum days. The cultures of show and lochia were taken from the vagina by separating the labia and inserting a sterile applicator for a distance of 2 centimeters. The vagina was not invaded to examine the cervix after the seventh month of pregnancy, unless under aseptic precautions in the hospital, and in each instance was for other obstetric complications, i.e., ruptured membranes, bleeding, etc., gonorrheal infection not being suspected. Two culture methods were employed,^{5*} but *Neisseriae* were reported positive only following a positive oxidase reaction, the presence of typical gram-negative diplococci from an oxidase positive colony, and typical sugar fermentation reactions. Smears were considered positive if gram-negative intracellular diplococci resembling the gonococcus were present. Patients were discharged from the hospital to the clinic, if urethral and cervical cultures were negative on three alternate days, beginning three days after termination of treatment. All patients were treated and followed for cure while isolated in the hospital, and were referred back for further treatment, if found to harbor organisms while under observation in the clinic.

*The specimen was collected on a sterile swab which was placed in 2 c.c. of sterile broth (2 per cent Difco proteose peptone No. 3 and 0.5 per cent NaCl) and distributed well in the tube. Chocolate agar (Difco Bacto-proteose No. 3 and Bacto-hemoglobin) was inoculated with the above suspension and was then smeared over the surface of the plate. Plates were incubated at 35 to 37 degrees Centigrade for 48 hours, in a chamber providing increased moisture and an atmosphere of 8 to 10 per cent carbon dioxide.

Fifty obstetric patients have been proved to harbor *Neisseriae* by cultural identification, and are presented with forty-four patients who had findings suggesting gonorrhea infection and/or positive smears, in an attempt to clarify certain problems encountered in the management of gonorrheal infection in pregnancy.

Duration and Condition of Pregnancy at the Time of Diagnosis

Seven patients were admitted as abortions, four being threatened, two complete, and one incomplete. Thirty-five patients had normal intra-uterine pregnancies with one being in the first trimester, eleven in the second trimester, and twenty-three in the third trimester. Three of the patients in the third trimester were admitted because of bleeding. Eight patients were diagnosed postpartum following term delivery. The average time of delivery was 34 weeks for all cases. Nineteen patients gave a history suggesting gonorrhea, and thirty-one patients denied knowledge of previous infection. Thirty-four patients enumerated suspicious symptoms, and sixteen patients denied symptoms. Forty-four patients had suggestive clinical findings, and six patients showed no evidence of urogenital infection.

Comparative Efficiency of Smear and Culture

The urethral smear was positive in 62 per cent, and the cervical smear positive in 73.3 per cent of patients. Thirty patients had both urethral and cervical smears, and each was positive in 69.5 per cent, and each was negative in 30.5 per cent of this group. The urethral culture was positive in 75 per cent, and the cervical culture was positive in 87.5 per cent of cases. Thirty patients had both urethral and cervical cultures, and both were positive in 46.6 per cent of cases.

Culture Control Group

Ten patients were cultured by two different methods.^{5*} There was complete agreement in seven patients and disagreement in three. One patient had negative smears and cultures to the first technique. She had an old cervical laceration with thin purulent discharge, and marked tenderness and induration in the right adnexa, with a history of previous pelvic inflammation and exaggeration of symptoms for two months, which was the duration of the pregnancy. Eleven days later, she had a positive cervical culture and negative urethral culture by the second technique. She was not checked again by either method. It is most probable that she had a chronic infection and was harboring gonococci of low virulence, or she may have acquired a new infection in the interval. The second patient had positive urethral and cervical smears, and the cervix was negative to the first culture method. The following day, she had positive urethral and cervical cultures to the second method, and was not checked again by the first method. She complained of frequency and burning on urination for ten days, had urethritis, cervicitis, purulent vaginal discharge, and an ulcer on the vaginal wall with a positive Kahn test. The third patient had negative urethral and cervical smears on admission to the clinic, and repeated negative urethral and positive cervical cultures by the first method. One week later, urethral and cervical cultures were negative by both methods as were subse-

*See preceding footnote.

quent cultures during the antepartum period. She delivered four months later, had a normal puerperium and infant, and subsequent cultures were negative. The two culture methods agreed accurately in 70 per cent of the cases.

Smear Control Group

This group was collected from approximately 2,500 obstetric admissions over a period of one year, and is comprised of 44 patients admitted in labor, at term, who had not been cultured previously. Thirty-seven of these patients had positive urethral smears and negative cultures. Three had positive urethral smears and negative cultures, and negative cervical smears and cultures. Four patients had negative urethral smears and cultures, and positive cervical smears and negative cultures. The cervical specimens were taken at the time of aseptic vaginal examinations. The lochia from 15 of these patients was cultured, and all were negative. Eleven patients had late postpartum morbidity, with positive urethral smears and negative urethral and lochial cultures. Three infants born of these mothers had nonspecific ophthalmia. Three patients had condyloma acuminata of the vulva and two had Bartholin abscesses.

Stage and Site of Infection as Proved by Culture

Thirty-one patients had evidence of acute infection, and in nineteen patients the infection appeared to be chronic. Only the urethra was positive in twenty-two patients, and only the cervix in fourteen. Both the urethra and the cervix were positive in fourteen patients.

Associated Diseases

Five patients had primary syphilis, two late syphilis, one lymphopathia venereum, and of those patients examined for trichomonads, three were positive. Four patients had Bartholin abscesses, one Skenitis, one granuloma inguinale, five condyloma acuminata, two thrush vaginitis, and one patient had chronic salpingitis. One patient had acute arthritis thought to be caused by the gonococcus.

Treatment

Forty-four of the 50 patients with positive cultures were treated, and thirty-eight were negative after the first course. Six remained positive after the first course and received subsequent treatment. Three different therapeutic approaches were employed:

1. Sulfonamides orally, chiefly sulfathiazole, using approximately 40 grams in eight days. Eighteen patients were treated and sixteen were negative after the first course. One patient was negative after two courses, and one patient after three courses of treatment.

2. Local application was made to the vulva, vagina and cervix of an ointment containing 2 per cent allantoin, 15 per cent sulfanilamide, and 5 per cent lactose in a special greaseless base buffered to a pH of 4.5 with lactic acid.⁶ This method was used only in patients who had positive cervical and negative urethral cultures, and was applied twice daily for ten days. Nine cases were treated, and eight were negative after the first course. One patient required a second course of treatment and remained negative thereafter.

3. A combination of the two afore-mentioned methods was employed in seventeen cases, and fourteen patients were cured after the first course, two after a second course, and one patient was still positive after two subsequent courses of local treatment. She then received another course of combined treatment and was negative. She was again positive in the clinic before delivery and probably was reinfected.

Sulfonamide blood levels were adequate in most cases, and adequate in those treatment failures in which levels were recorded. Patients on local treatment never had more than 1 mg. of sulfanilamide per 100 c.c. of blood.

There were four morbid patients and all occurred in the first few days post partum. There was no morbidity in the antepartum patients. Bed rest was insisted upon, even in the ambulatory antepartum patient, and was considered an important part of the therapy.

Condition of Mothers and Infants Following Delivery

Forty-three of the 50 culture-positive patients were delivered in hospitals, but only 27 were delivered in Gallinger Municipal Hospital. Twenty-six mothers delivered 26 premature and mature infants, and one patient delivered a previable infant. Eleven infants were males, and 15 were females. It was interesting to note the absence of genital disease in all infants. Two infants developed ophthalmia, both were gonococcal and subsequent cultures from the mothers were positive. The urethral smears from these mothers were negative on admission, but later urethral smears and cultures were positive post partum. One infant developed jaundice, two diarrhea, and one died of pneumonia. Twenty-four mothers were followed in the hospital after delivery for evidence of infection, and of this number, eight were diagnosed for the first time and treated, before follow-up. Two patients treated previously were positive to culture after delivery. Both had been treated adequately and confined continuously to the hospital subsequent to treatment and prior to delivery. Gonococci were recovered from the urethra in both patients. The first patient had positive urethral and cervical cultures after sulfathiazole. She was then treated with sulfanilamide, and had a negative culture from the urethra on day of delivery. The urethral culture was again positive on the seventh day post partum. The second patient had negative urethral and cervical cultures 14 days prior to delivery, and the urethral culture was positive 9 days after delivery. The show and lochia were negative in both cases, and both patients were considered cured following the succeeding course of treatment. The average time between diagnosis and delivery for 17 cases was 79 days. The greatest number of days between diagnosis and delivery was 225, and the fewest that of delivery.

Discussion

Since a positive diagnosis was based on isolation of *Neisseriae* from either the urethra, cervix, or both, 100 per cent of the 50 patients were positive to culture. Seventy-four per cent of patients had either positive urethral, or cervical smears, or both, and might have been diagnosed by smear alone. However, if smear alone had been used, 26 per cent of the cases positive to culture would have been missed. On the other hand, if only smear had been used for diagnosis in both the culture-positive

group (50 patients), and the smear positive-culture negative group (44 patients), 26 per cent of the culture-positive cases would have been missed, and 100 per cent of the smear positive-culture negative cases would have been falsely diagnosed positive. Thus, the state of confusion resulting from the use of smear and culture in the diagnosis of gonorrhea is explained. To corroborate the diagnosis by smear in the smear positive-culture negative group, eleven patients had late postpartum morbidity, three condyloma acuminata of the vulva, two Bartholin abscesses, all being suggestive clinical evidence of gonorrheal infection.

In the culture-control group, there was complete agreement in 70 per cent of the ten cases. In the three which disagreed, two cases can be eliminated because of a time interval between the two techniques, seven days in one case, and 11 days in the other. Both methods would have been positive in the third patient, if they had been repeated. Van Slyke, Thayer, and Mahoney report the findings of several laboratories using identical culture media, comparable inoculation techniques, and the use of identical secretions in 140 gonococci-positive culture cases. The closest any two laboratories could check on any medium was 75 per cent of the cases.⁷

While it is evident that culture is more efficient than smear in establishing a positive diagnosis, it has pitfalls. These are, in the main, dependent upon the virulence of the gonococcus, the manner in which specimens are obtained and stored prior to incubation, and the media and method of incubation employed. Nothing will be said of the difficulties encountered in cultural technique, but certain observations relating to the biology of the gonococcus can be utilized to increase the efficiency of culture. It was necessary to repeat cultures several times in several different patients before the gonococcus was isolated. This was done because the history and findings were suspicious. One patient had repeatedly positive smears, and the culture was not positive until repeated three times. The smear will occasionally reveal the presence of an intracellular diplococcus whose virulence is so reduced that it will not grow out on artificial media until activated, and can be recovered later, if a suspicious or positive smear has kept the examiner on the alert. The difficulty with smear is that it is also positive with a great variety of organisms other than *Neisseriae* which compose the flora of the female genital tract.^{1, 4, 8, 9} The chief offenders are the species of the tribes *Streptococceae*, *Staphylococceae*, *Mimeae*, coccoid forms of the colon bacillus, and the gram-positive diplococcus which tends to lose the strain. It is important that an exhaustive examination be made of the vulva, urethra and adjacent ducts, the vagina, cervix and adnexa, and that specimens obtained at this examination, be used for smear and culture. The lower portion of the urethra should be expressed outwardly, and the contents of the cervical glands expressed by gently grasping the cervix between the blades of the speculum. Douching or voiding before collec-

tion of specimen,¹⁰ will wash away or inhibit in some manner, the growth of the organisms. Thick lubricating jellies lead to errors in diagnosis,¹¹ probably by inhibiting growth, or mechanically interfering with proper plating of the specimen.

Very little difficulty was encountered in establishing a diagnosis in the acute infection, both the smear and culture being positive in the presence of acute inflammation. In the treated patient, or one harboring a chronic infection, the diagnosis was more difficult. The gonococcus may be deeply embedded in the glandular structures of the urethra and cervix, its virulence reduced, with only a mild chronic inflammatory reaction in the structures involved.

Three patients at term, in labor, were examined vaginally for obstetric complications, and the unsuspected cervix found infected. There was no history of infection, no suggestive symptoms, and no findings other than a cervicitis. Both the urethra and cervix should be examined in patients with a suspicious history or findings, even after the seventh month of pregnancy, but should be done with aseptic precautions. Aqueous Zephiran 1:1,000 was instilled into the vagina following examination, and was considered a valuable procedure.

Two patients were found to have infections from which *Neisseria catarrhalis* was isolated. One patient was five months pregnant when diagnosed. The urethral and cervical smears showed typical gram-negative intracellular diplococci, and cultures from both sources subjected to fermentation studies revealed this organism. She had a mild urethritis and cervicitis, was treated with sulfathiazole by mouth, with clinical improvement and negative cultures. Five weeks later, she had a yeast vaginitis with negative cultures for *N. catarrhalis*. Four weeks later, cultures for yeast were negative but *N. catarrhalis* was again obtained from the urethra and cervix, which were mildly inflamed. She delivered at another hospital, and did not report back for follow-up. The second *N. catarrhalis* infection was found post partum, and was of no particular interest.

The gonococcus was not recovered from cultures of show and lochia. Since lochia possesses certain properties favorable to the artificial growth of this organism, i.e., serum with high hemoglobin content, alkaline reaction, and is incubated in the human body at optimum temperature in a moist anaerobic environment, it was anticipated recovering the organism in some cases. The proper pH for artificial growth of the gonococcus is (7.2 to 7.6),⁴ so an increased alkalinity of the lochia may be lethal as the gonococcus is destroyed rapidly in culture media with a pH above 8. Perhaps, the innumerable bacteria in the vagina of the gravid and puerperal woman may overgrow the more delicate gonococci⁵ on artificial media.

In ten postpartum patients, the gonococcus was recovered from the urethra. Eight were diagnosed for the first time, and two had been

previously diagnosed and treated. This is in accord with Dr. Curtiss who believes the urethra is often the site of persistent gonorrheal infection, and infections of the cervix less persistent than he formerly thought.¹

Gonorrheal infection seemed more persistent and resistant to treatment in pregnancy. Six of the forty-four patients treated were still positive after the first course of treatment. Four of these six patients had negative cultures after two courses of treatment. One patient had negative cultures after three courses of treatment, and a single patient was still positive after a third course. It is impossible to be certain when a patient is free of infection following treatment, but in the light of present knowledge, patients should be followed closely for four to six months with frequent smears, cultures, and clinical evaluation. If there is no evidence of infection after this period, it is probable the patient no longer harbors the gonococcus.

Four patients were morbid in the first few days after delivery. Dr. DeLee states: "Acute infections are likely to show the exacerbation in the first few days of the puerperium, because of the associated streptococci and staphylococci while chronic gonorrhea causes the 'late fevers' in pus tubes or adhesive obliterating peritonitis, often, not always, leaving permanent sterility, and gynecologic invalidism."² As nearly as these four patients can be classified correctly at time of delivery, two had acute infections and two were cured, and will be discussed in that order. The first case was admitted at the ninth month of pregnancy, in active labor with a history suggesting infection. She had a Bartholin abscess, purulent urethral discharge, with a positive urethral smear and negative urethral culture. The urethral culture was repeated on the second postpartum day, when patient had an elevation to 102 degrees Fahrenheit and was positive. She was treated and subsequent cultures were negative. The second patient was admitted as an early abortion at the second month of pregnancy, and urethral smear was negative. She continued to bleed and sponge stick curettement of uterus was done. She was febrile on the second postpartum day, and urethral culture taken at this time was positive. She responded to sulfathiazole and subsequent cultures were negative. The third patient had a positive urethral culture at the sixth month of pregnancy, was treated and considered cured. She delivered at the tenth month, and was morbid from the third to the seventh postpartum days. Her cultures were negative for *Neisseriae* post partum. The fourth patient had a positive cervical culture when eight and one-half months pregnant. She was treated and subsequent cultures were negative. She delivered six weeks later, and was morbid on the third and fourth postpartum days. Urethral, vaginal, and later cervical cultures were negative for *Neisseriae*. There was no evidence of adnexal disease in any of these patients on discharge from the hospital. Both the acute and cured infections were morbid in

the first few days after delivery. In the two acute infections, gonococci were recovered from the urethra shortly after labor. In the two cured infections, considerable time had elapsed since treatment. The urethra was positive in the two acute infections, and had been positive in one cured infection. Only the cervix had been positive in the second cured infection. Apparently, the morbidity in the two cured infections was caused by organisms other than *Neisseriae*. In the control group by smear, eleven patients had late postpartum morbidity with positive urethral smears, and negative urethral and lochial cultures.

The author believes diagnosis by smear is more misleading in the pregnant patient though a comparative study was not made. The characteristic changes in the tissues of the pelvis in pregnancy, i.e., hypertrophy, softening, increased vascularity and glandular activity with increased hydrogen ion concentration of the vagina, inhibit the growth of certain organisms. But if the vagina or cervix become eroded, or there is abnormality of the secretion in the vagina, all sorts of organisms may be found which can cause confusion. A latent gonorrheal infection in the urethra or cervix may be stimulated by the changes of pregnancy, and a discharge recur from which gonococci can be isolated. In the pregnant patient, the vagina and vulva are frequently involved in the acute inflammatory process giving rise to more clinical evidence of disease.

Summary and Conclusions

Fifty obstetric patients have been examined by smear and culture in the antepartum, intrapartum, and postpartum periods and proved to harbor *Neisseriae* by cultural identification. Forty-four obstetric patients at term, in labor, with findings suggesting gonorrheal infection and/or positive smears but negative cultures, have been compared with the *Neisseria* positive group to demonstrate certain features relating to diagnosis, treatment, and management of *Neisserian* infection in pregnancy.

1. Culture is more efficient than smear in establishing a positive diagnosis in *Neisserian* infection in pregnancy.

2. Smear is valuable in conjunction with culture in establishing a positive diagnosis in chronic infections, and particularly in following treated patients for cure.

3. Repeated smear and culture at the time of a searching physical examination is the most adequate method of diagnosis. One negative smear and culture will not rule out gonorrhea.

4. *Neisseria catarrhalis* was isolated from 4 per cent of the patients. In the interest of an accurate diagnosis, and for the protection of patient and physician, fermentation studies should be done to identify the particular *Neisseria* present.

5. The gonococcus was apparently activated by the trauma of labor, and recovered from the urethra post partum, in two treated patients who had negative cultures before labor.

6. The gonococcus was recovered from the urethra of eight postpartum patients not previously diagnosed or treated.

7. The gonococcus was not recovered from the show or lochia of patients proved to harbor the infection in the urethra or cervix.

8. Two patients with acute gonorrhea, and two with cured infections had early postpartum morbidity with clinical endometritis.

9. Gonorrheal infection appeared more persistent and resistant to treatment in pregnancy.

10. Diagnosis by smear seemed more confusing in the pregnant than in the nonpregnant female.

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References

1. Curtiss, A. H.: A Text Book of Gynecology, 3 ed., Philadelphia, 1939, W. B. Saunders Co.
2. DeLee, J. B.: The Principles and Practice of Obstetrics, 7 ed., Philadelphia, 1939, W. B. Saunders Co.
3. Beck, A. C.: Obstetrical Practice, 2 ed., Baltimore, 1939, The Williams and Wilkins Co.
4. Pelouze, P. S.: Gonorrhea in the Male and Female, 3 ed., Philadelphia, 1939, W. B. Saunders Co.
5. DeBord, G. G.: Descriptions of Mimeae, Trib. Nov. With Three Genera and Three Species and Two New Species of Neisseria From Conjunctivitis and Vaginitis, Iowa State College J. Sc. 16: 471-480, 1942.
6. Parks, John: The Treatment of Infections of the Cervix, Vagina, and Vulva With an Allantoin-Sulfanilamide-Lactose Ointment, Ann. District of Columbia 12: 175-177, 1943.
7. Van Slyke, C. J., Thayer, J. Duward, and Mahoney, J. F.: Comparison of Media and Laboratory Results in Gonococcus Culture, Am. J. Syph., Gonor. & Ven. Dis. 26: 55-62, 1942.
8. Sulkin, S. Edward, and Gottlieb, Eleanor: The Use of an Improved Culture Medium in the Diagnosis of Gonococcal Infections in the Adult Female, Am. J. Syph., Gonor. & Ven. Dis. 25: 22-27, 1941.
9. DeBord, G. G.: Species of the Tribes Mimeae, Neisserieae and Streptococceae Which Confuse the Diagnosis of Gonorrhea by Smear, J. Lab. & Clin. Med. 28: 710-714, 1943.
10. Lewis, R. M.: Management of Gonorrhea in the Female, Am. J. Syph., Gonor. & Ven. Dis. 27: 418-427, 1943.
11. Gillick, Frederick G., Sulkin, S. Edward, and Stephens, LeRoy J.: A Common Error in Obtaining Specimens for the Cultural Diagnosis of Gonococcal Infections in Women, Ven. Dis. Inform. 21: 288-290, 1940.

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CORTICAL NECROSIS OF KIDNEYS ASSOCIATED WITH NECROSIS OF PITUITARY IN OBSTETRICAL SHOCK

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POSTPARTUM necrosis of the anterior lobe of the pituitary gland has been described numerous times and is becoming a well-known clinical entity. Likewise, the occurrence of bilateral renal cortical necrosis in pregnancy, in shock, in infections, and of undetermined origin has been described. No cases are found in the literature available describing a combination of necrosis of the anterior lobe of the pituitary gland and bilateral renal cortical necrosis following parturition. It is the object of this paper to report such a case.

Case Report

The patient, a white female, aged 28, married, was first admitted to the hospital on July 14, 1942, when she had a spontaneous delivery of an anencephalic monster of 8 months' gestation. There were no complications during the pregnancy or delivery. At this time she had one child, aged 22 months.

She was next seen at the outpatient obstetrical clinic June 16, 1943; her last menstrual period was April 17, 1943, and the estimated date of confinement was January 24, 1944. Physical examination at this time was normal. She attended the clinic regularly and September 20, 1943, was admitted to the hospital for back pain and nocturia of one day's duration. Physical examination was negative. Hemogram revealed hemoglobin 70 per cent (Tallqvist), 3,850,000 erythrocytes, 7,250 leucocytes; differential, 74 neutrophils, 1 eosinophile, and 25 lymphocytes. Blood serology was negative. Urine analyses for this admission are given in Table I.

TABLE I. URINE ANALYSIS, SEPTEMBER, 1943, ADMISSION

DATE	ALBUMIN	SUGAR	MICROSCOPIC			CATHETERIZED
			CASTS	PUS CELLS	BLOOD CELLS	
9/20	+	0	0	++++	0	No
9/21	0	0	0	++++	0	Yes
9/22	0	0	0	++++	0	No
9/23	0	-	0	++	+	Yes
9/25	++	0	0	-	++++	No
9/26	0	0	0	0	++++	No
9/27	0	0	0	0	0	No
9/28	0	0	0	0	0	No

She received sulfadiazine until hematuria appeared on September 24, 1943, when it was stopped and mandelic acid therapy was started. She was discharged on September 28, 1943, with a diagnosis of pyelocystitis (right) of pregnancy. Following discharge, she was followed in the clinic with no recurrences or further difficulties until she returned to the

hospital on December 25, 1943, with fever, pain and tenderness in the right costovertebral angle of two days' duration. Temperature on admission was 102° F., rapidly falling to normal in two days. Hemogram was hemoglobin 65 per cent (Tallqvist), 3,450,000 erythrocytes, 5,250 leucocytes; differential was 68 neutrophils, 2 eosinophils, and 30 lymphocytes. The urine on admission showed three-plus pus cells with a few erythrocytes, no albumin, and it continued to show pus cells, but no more erythrocytes. She was placed upon sulfadiazine on admission with good response. Due to the holidays, the patient insisted upon discharge and went home December 31, 1943.

Her last admission was on January 6, 1944, with complaint of cough, backache, fever, and sordes of mouth. Her condition had been fair during the interval, and the day of admission was the first time she had a fever (100° F.).

Physical examination revealed multiple sordes of the tongue and mouth. Heart and lungs were negative. Blood pressure was 120 mm. of mercury systolic, and 80 mm. of mercury diastolic. The uterus was two fingerbreadths below the xiphoid, deflected to the left, with the buttocks in the fundus and soft parts to the right. The head was floating above the symphysis. Fetal heart rate was 140 per minute. Chest roentgenogram was negative. Sedimentation rate was 90 mm. per hour (Westergren). Blood serology was negative. The clinical laboratory data are tabulated in Table II.

Course in Hospital.—The patient ran a fairly even course on January 7, 8, and 9, with her temperature gradually climbing to 103° F., when she was placed on a sulfadiazine routine.

January 10.—Temperature 104° F. Few uterine contractions, head not engaged, fetal heart fast. Transfusion (citrate method) of 500 c.c. of blood at 2 P.M., with no reactions.

January 11.—Temperature 103.5° F. Condition unchanged.

January 12.—Temperature 103° F. Fetal heart tones have disappeared, and cervix was dilating slowly. Sulfadiazine discontinued.

January 13.—Taken to operating room at 9:50 A.M. and under ether and ethylene anesthesia midforceps extraction of a female stillborn child was performed at 10:12 A.M. with an episiotomy. The placenta was not expelled, and was manually removed in fragments at 11:20 A.M. It was estimated that the blood loss did not exceed 300 cubic centimeters. The patient went into severe shock, almost dying on the table, and was given blood, plasma, fluids, and cardiorespiratory stimulants. Blood pressure was not recorded in operating room; on return to ward it was 90 mm. of mercury systolic and 60 mm. of mercury diastolic. At 10:00 P.M. blood pressure was 95 mm. of mercury systolic and 60 mm. of mercury diastolic and the patient was comatose.

January 14.—The patient vomited at intervals. Temperature fell from 101° F. at 1:00 A.M. to 97° F. at midnight and 96° F. at 4:00 A.M. the following morning.

January 15.—Vomiting, drowsy, condition critical. Anuric. Ureters lavaged, but no crystals were obtained, and no obstruction was encountered.

January 16.—Patient almost totally anuric. Blood pressure 120 mm. of mercury systolic and 72 mm. of mercury diastolic. Involuntary liquid stools today.

TABLE II. CLINICAL LABORATORY DATA, LAST ADMISSION

DATE	URINE				HEMOGRAM							BLOOD CHEMISTRY					ICTERUS INDEX
	color	appearance	reaction	specific gravity	albumin	casts	pts. cells	blood	crystallized	hemoglobin (% sat'd)	erythrocytes (millions per c.m.m.)	leucocytes (thousand c.m.m. per c.c.)	neutrophils	eosinophiles	basophiles	lymphocytes	
1/6 1911	amb.	cloudy	acid	1.012	++	0	loaded	+	no	56	2.85	7.6	53	3	1	41	NONPROTEIN NITROGEN (MG. PER 100 C.C.)
1/7					+	0	+++	+	yes								(MG. PER 100 C.C.)
1/8																	CREATININE (MG. PER 100 C.C.)
1/9																	(MG. PER 100 C.C.)
1/10	yel.	cloudy	acid	1.017	0	0	+	+	no	50	3.06	5.2	62	3	1	35	GLUCOSE (MG. PER 100 C.C.)
1/11	amb.	cloudy	acid	1.015	-	0	loaded	0	no	50	3.15	4.6	60	3	1	36	(MG. PER 100 C.C.)
1/12	amb.	cloudy	acid	1.015	+	0	loaded	0	no	56	3.24	5.0	63	3	1	35	SULFADIAZINE (MG. PER 100 C.C.)
1/13	Delivery 1/13/44 at 11:20 A.M.	cloudy	acid	1.014	+	0	+	+	no		2.36	5.2					13.5 15.0
1/14	amb.	cloudy	acid	1.010	+	few gran.	+	+	no	42							
1/15	anurie																80.0
1/16	red	smoky	acid	1.008	++	0	0	all	no	36	1.70	4.0	62	12	1	36	50.0
1/17	red	smoky	alk.	1.009	++	0	0	blood	no	36	1.65	3.7	61	12	1	37	90.0
1/18	red	smoky	acid	1.012	++	0	0	blood	no	26	1.46	9.0	73	9	1	24	9.9
								all	no	20	1.27	19.0	62	9	1	35	9.9

January 17.—Voided 80 to 100 c.c. of urine. Some dyspnea and cyanosis present. Given oxygen.

January 18.—Still partially anuric (voided 250 c.c. in twelve hours). Condition very grave.

January 19.—At 2:00 P.M. a transfusion of 500 c.c. of blood (citrate method) was given, with no reaction. The patient expired at 6:13 P.M.

Autopsy Findings.—The body weight was 128 pounds and length, 66 inches. The breasts were engorged and milky fluid was easily expressed. There was massive perineal ecchymosis and a posterior episiotomy suture line.

The brain showed no gross softening, congestion, or hemorrhage. The ventricles were not dilated. Cerebrospinal fluid was clear and of normal amount. The pituitary gland was swollen, tense, and impinging on the infundibulum. It measured 2.3 by 1.5 centimeters. Following fixation in formol-alcohol, sectioning revealed a narrow 2 to 3 mm. rim of darker viable tissue around the anterior lobe surrounding the central soft, yellow-white, necrotic area (Figs. 1 and 2). The sella turcica showed no enlargement.



Fig. 1.—Cut surface of anterior lobe of pituitary gland showing central necrosis. (Formol-alcohol fixation.) (Magnification $\times 6$.)

There were no gross changes in the throat or neck. The thyroid was symmetrical and weighed 35 grams. The pleural spaces were clear. The lungs showed congestion with terminal bronchopneumonia involving the upper and middle lobes of the right lung. There were no infarcts and the pulmonary artery contained no emboli.

There was no increase in pericardial fluid. The heart weighed 300 grams and showed no gross changes or anomalies. The aorta was smooth, elastic, and showed no stenosis or dilatation.

There were no adhesions or increased fluid in the abdominal cavity. The liver protruded 4 cm. below the costal border. The diaphragm was not elevated. The liver was tense, pale red brown, and the cut edges bulged. There was no gross hemorrhage or infection.

The spleen was congested, swollen, and soft; it weighed 320 grams. The capsule was smooth, blue purple; the cut surface was dark, soft, and semifluid. There was no gross hemorrhage, infarction, or infection.

The pancreas and adrenals showed no gross changes.

The kidneys weighed 340 grams combined. There was moderate dilatation of the right ureter and pelvis with minimal dilatation on the left. There was no ureteral obstruction demonstrable in situ. The mucosal ureteral surfaces were edematous, yellow, and mucoid, but no hemorrhage, debris or crystals were present. They each contained 6 c.c. of yellow, thick urine; culture of this revealed organisms of the genus *Aerobacter*. The kidneys showed multiple confluent areas of yellow-white cortex surrounded by zones of hyperemia. The capsules stripped easily, seeming to be lifted by subcapsular fluid. The cut surfaces showed zones of yellow-white cortex surrounded by hyperemic tissue (Fig. 2). The necrotic areas had lost all the usual cortical markings except where there was a narrow 1 to 2 mm. zone of viable tissue supplied by capsular vessels. In areas, the columns of Bertini were dark red brown, and seemed to be the sites of some hemorrhage and central necrosis. There were no grossly recognizable thrombosed vessels present. There was slight blunting of the papillae in the right kidney with very minor dilatation of the calices. The mucosal surfaces were moderately granular and hyperemic. No crystalline or amorphous deposits were present.

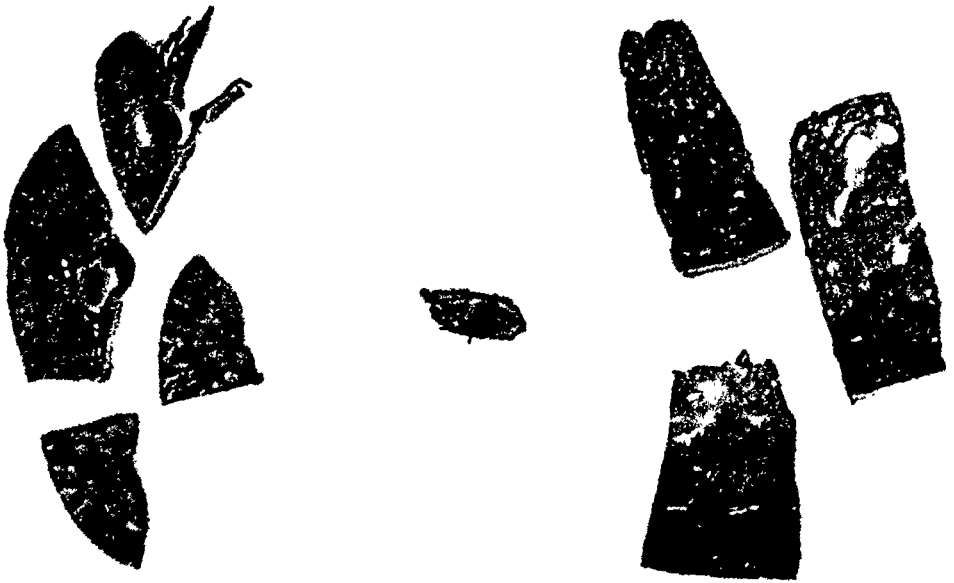


Fig. 2.—Cut surfaces of kidneys (left), anterior lobe of pituitary gland (center) and uterine wall (right). (Formol-alcohol fixation.) (Slightly reduced.)

The urinary bladder contained 10 c.c. of lemon-yellow, cloudy urine. The mucosa around the trigone was injected. There were multiple retro-peritoneal organized hemorrhages present around the bladder.

The uterus measured 25 cm. from fundus to cervical constriction, 20 cm. between the Fallopian tubes, and 12 cm. in depth at the midportion. The serosa was thickened, white, and free from exudate or hemorrhage. The Fallopian tubes and ovaries were normal, postpartum in character. There was marked hemorrhage beneath the peritoneal covering at the

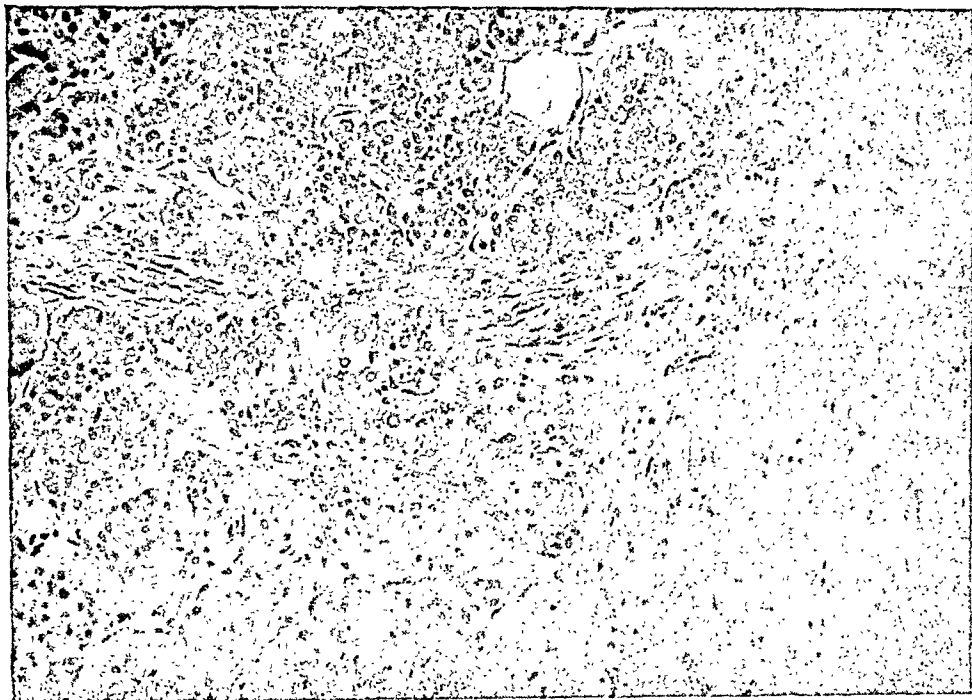


Fig. 3.—Section through edge of anterior lobe of pituitary gland showing viable cells and junction of necrosis. (Magnification $\times 800$.)

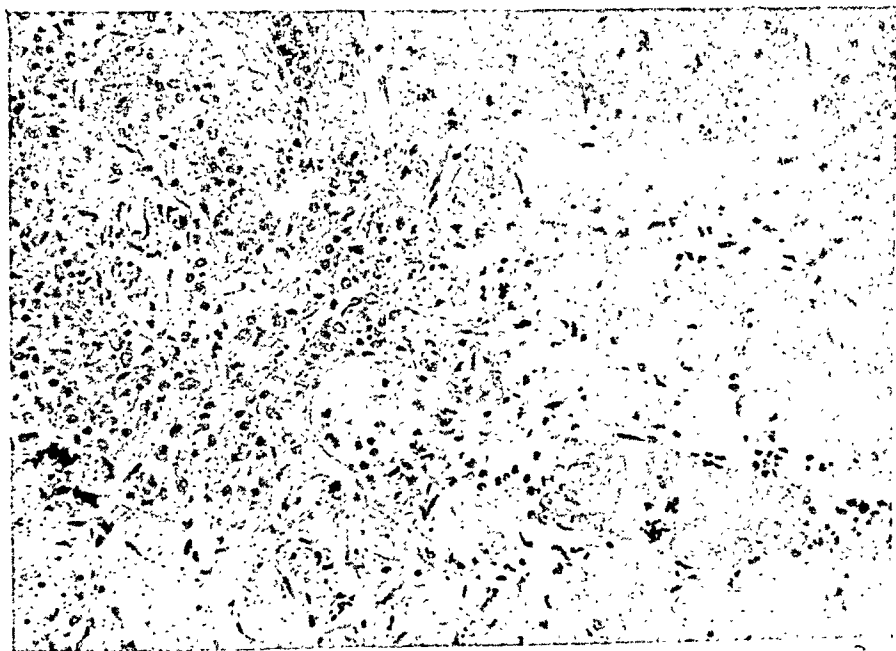


Fig. 4.—Section through necrotic area in anterior lobe of pituitary gland showing thrombosis of vessels. (Magnification $\times 800$.)

level of the internal orifice. This became confluent with hemorrhages in the vaginal walls and extended laterally and posteriorly to encompass the entire pelvis up to the sacral promontory. The uterine walls measured 1.5 to 2.0 cm. in thickness, and attached to the inner surface was a 2 to 3 cm. edematous, hemorrhagic mass of fibrin and fibrous-like tissue (Fig. 2). The sinuses in the uterine wall were dilated and filled with thick, unclotted blood. The external orifice was a ragged rim of hemorrhagic, torn tissue. The vaginal walls showed four incomplete vertical tears extending into, but not through the muscular layer. There was considerable hemorrhage into the rectovaginal septum with extension into the ischiorectal fossae.

There were no gross changes in the gastrointestinal tract.

Microscopic examination of sections from the brain, thyroid, heart, adrenals, pancreas, intestine, diaphragm, and skeletal muscle showed no noteworthy histologic changes. The liver sections showed minor congestion with no inflammation or degeneration. The lung showed an early bronchopneumonia.

Sections from the anterior lobe of the pituitary gland showed a rim of congested viable pituitary cells in which typical acidophilic "pregnancy cells" were present (Fig. 3). The viable cells surrounded a large area of acellular debris representing ischemic necrosis of the major portion of the gland. In these areas, shadowy outlines of cells could be seen surrounding small thrombosed arteries and veins (Fig. 4). Away from these areas, the endothelial spaces were mostly collapsed, but in a few thrombosis was easily recognized. There was no evidence of infection or tumor.

Sections of the kidneys showed an abrupt transition from viable to necrotic areas in the cortex. The necrosis was complete and only shadows of cells could be seen. The general architecture remained and the vessels were engorged with some necrosis of their walls and occasional rupture (Fig. 5), especially of the intralobular arteries which almost always contained thrombi. The glomeruli were pale, necrotic in such areas, and it was possible to trace a thrombus from an afferent arteriole (Fig. 6), back to its (the afferent arteriole) intralobular origin. There was a marked absence of inflammatory reaction or exudate in the necrotic areas, but hyperemia, exudate, and edema surrounded such areas. The tubules showed granular and cellular debris with some casts. In areas of the kidney that were not grossly necrotic, there was a very minor inflammatory reaction along the tips of the papillae and the mucosal surfaces. There was no evidence of glomerulonephritis or of interstitial nephritis.

Sections from the uterus showed the usual muscle hypertrophy with edema and congestion. No endometrial structures could be seen. The approximate region of the endometrial base faded into edematous eosin-staining fibrillar structures with no nuclear or cytoplasmic outlines. No histologic evidence of placenta accreta could be seen. There was a remarkable lack of inflammatory or phagocytic activity in these sections.

Gross and microscopic examination of the stillborn baby in this case showed no evidence of changes beyond some intrauterine maceration and forceps marks on the head.

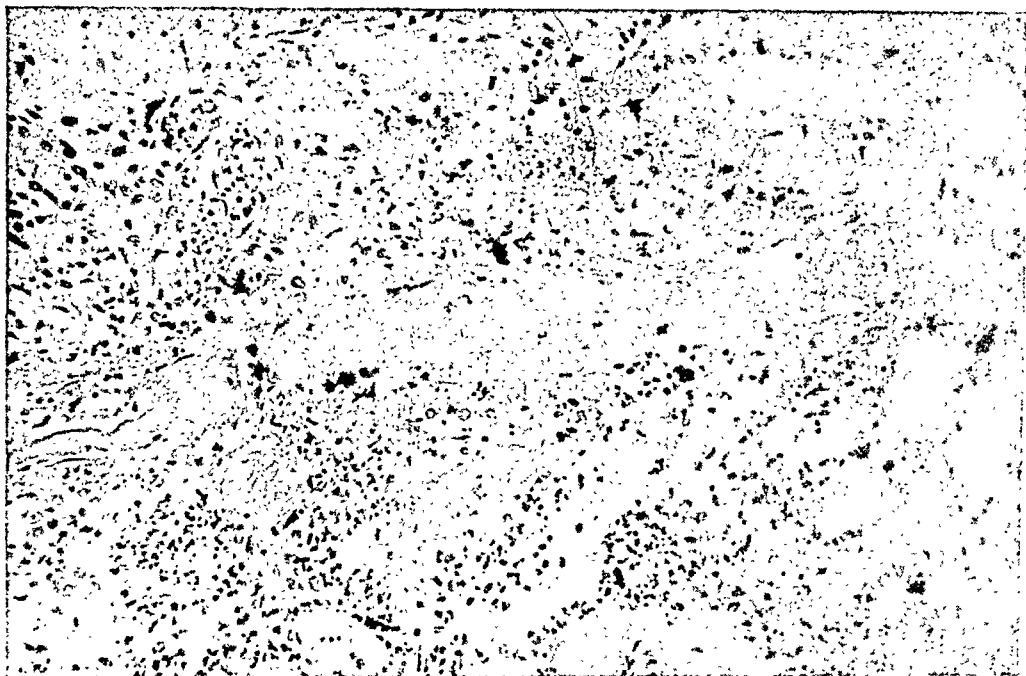


Fig. 5.—Section of kidney showing thrombosis and rupture of an intralobular artery. (Magnification $\times 800$.)

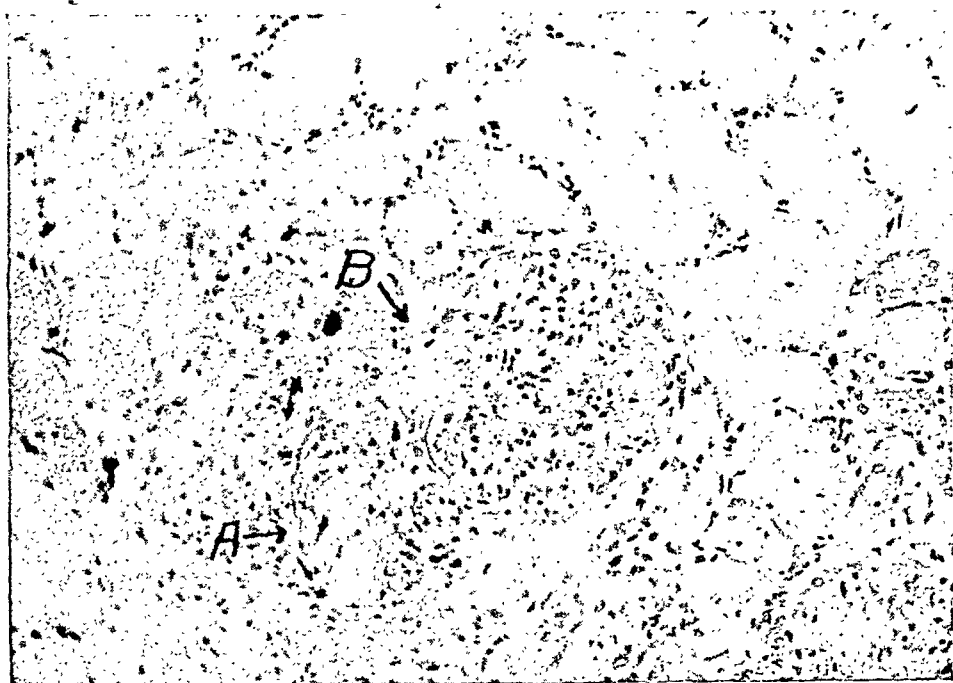


Fig. 6.—Section of kidney showing thrombosis of afferent arteriole at A, entering thrombosed glomerulus at B. (Magnification $\times 800$.)

Discussion

Numerous case reports¹⁻⁴ have been published of postpartum necrosis of the anterior lobe of the pituitary gland following Sheehan's⁵ first paper reporting 11 cases studied at autopsy, and he has summarized the reported autopsy cases in another later paper.⁶ From his studies, he believes that the necrosis starts about the time of delivery, is due to thrombosis and not embolism of the pituitary sinuses, and is usually consequent upon the collapse of the patient following severe hemorrhage often as a result of a retained placenta. Such factors were certainly present in the case reported here.

Hutchinson⁷ reported a case of necrosis of the anterior lobe of the pituitary gland during pregnancy in which the patient was approximately two months pregnant. At autopsy a pulmonary embolus probably from septic endometritis was found along with necrosis of the anterior pituitary gland. In this case there was no hemorrhage, but the patient was in extreme shock following the pulmonary embolus, and expired approximately forty hours later. The histologic picture of the necrotic pituitary gland was estimated to be of thirty-six to forty hours' duration following the criteria set forth by Sheehan.⁵

Ash⁸ has summarized the literature on bilateral cortical necrosis of the kidneys up to 1933. Of the 44 authentic cases he collected, 34 complicated pregnancy, and of the 18 cases about which there might have been some question, 8 were in pregnancy, giving a total of 62 possible cases, with 42 of these occurring in pregnancy. He states from this material: "The evidence indicates that the thrombosis is secondary, not to the necrosis, as some would claim, but to the stasis. The thrombi begin in the afferent arteries and extend in a proximal direction to the limit of the necrosis, so that they rarely go beyond the interlobar arteries. They are rare in the glomeruli, efferent arteries and veins. The blood in these vessels is 'stale' and so may have lost some of its coagulability. The exudate does not represent a primary inflammatory reaction as much as it does the reaction to necrotic tissue."

De Navasquez⁹ feels that the kidneys prior to the onset of symmetrical cortical necrosis of pregnancy are histologically normal and the primary change is necrosis of the peripheral intralobular arteries producing ischemia, and necrosis with the thrombosis being a terminal picture resulting from the stasis thus produced. He reports 12 additional cases associated with pregnancy.

Dunn and Montgomery¹⁰ feel that extreme glomerular capillary dilatation with loss of plasma producing inspissation of the blood and blocking of the circulation at this level is the ultimate factor in bilateral cortical necrosis. He feels it is possible to classify the condition as follows: "(I) Inflammatory, in acute necrotizing glomerulonephritis; (II) ischaemic, in the cortical necrosis of the renal toxæmias of pregnancy; and (III) venostatic, in acute thrombosis of the renal vein."

Godwin and McCall¹¹ reported a case of bilateral cortical necrosis of the kidneys in a man who died with peritonitis following perforation of a gastric ulcer. They felt that bacterial toxins were probably responsible for the cortical necrosis, but that shock with its resulting capillary stasis might have been a contributing factor.

McFarlane¹² describes a typical case of bilateral renal cortical necrosis that followed multiple fractures with internal hemorrhage, and he was

sure that any bacterial or toxic factor could be excluded, and that shock was the direct cause.

Penner and Bernheim¹³ in a series of experiments with dogs produced severe shock by the intraperitoneal and intrapleural injection of epinephrine hydrochloride. In some of their animals, they found cases of bilateral cortical necrosis of the kidneys which were similar to those that had been reported in human beings and to the human cases they had studied. They felt that the vasospasm which occurs in shock was of sufficient intensity and duration to result in the kidney lesions in some instances.

In the case reported here, there were no signs of eclampsia and no autopsy evidence of the usual toxemias of pregnancy. The patient had a severe operative delivery with considerable frank bleeding, and more concealed bleeding internally. Severe shock developed and following this anuria, drowsiness, fall of temperature, and a persistent hypotension occurred. There was a steady rise in the nonprotein nitrogen and creatinine, with onset of vomiting and diarrhea. The gradual loss of hemoglobin and erythrocytes must have occurred as a result of bleeding from the kidneys, inasmuch as the icterus index was not elevated and there were no other bleeding points.

Summary

In the case reported here, there was combined necrosis of the anterior lobe of the pituitary gland and the cortices of the kidneys. The histologic picture of the pituitary and kidney changes was compatible with five to six days' thrombosis. The clinical picture was typical, and no evidence of other factors was found at autopsy. The collapse and shock at delivery was extreme, and it is felt that the changes found were initiated then. Added support is given to the belief that postpartum necrosis of the anterior lobe of the pituitary gland and bilateral renal cortical necrosis may be caused, in many instances, by severe shock in reporting here a case showing both of these conditions occurring simultaneously in the same patient.

References

1. Gotshalk, H. C., and Tilden, I. L.: *J. A. M. A.* 114: 33, 1940.
2. Brown, Clark E., and Eder, Lawrence F.: *Am. J. M. Sc.* 198: 166, 1939.
3. Reekie, R. D.: *West. J. Surg.* 50: 293, 1942.
4. Cunningham, J. F., McGrath, J., O'Donovan, D. K., and de Valera, E.: *Irish J. M. Sc.* 519, September, 1942.
5. Sheehan, H. L.: *J. Path. & Bact.* 45: 189, 1937.
6. Sheehan, H. L., and McLetchie, N. G. B.: *J. Obst. & Gynaec. Brit. Emp.* 50: 27, 1943.
7. Hutchinson, H. E.: *J. Path. & Bact.* 51: 442, 1940.
8. Ash, J. E.: *Am. J. M. Sc.* 185: 71, 1933.
9. De Navasquez, S.: *J. Path. & Bact.* 41: 385, 1935.
10. Dunn, J. S., and Montgomery, G. L.: *J. Path. & Bact.* 52: 1, 1941.
11. Godwin, B., and McCall, A. J.: *Lancet* 2: 512, 1941.
12. McFarlane, D.: *J. Path. & Bact.* 52: 406, 1941.
13. Penner, A., and Bernheim, A. I.: *Arch. Path.* 30: 465, 1940.

MASSIVE OBSTETRIC HEMORRHAGE REQUIRING HYSTERECTOMY*

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ACCUMULATING evidence²⁻⁴ indicates that obstetric hemorrhage is now the most important and perhaps the most frequent cause of maternal mortality. Faulty or delayed obstetric hemostasis and the failure properly to replace the volume of blood which has been lost through hemorrhage are responsible for the mortality in most of these cases.

Simple and well-known conservative obstetric procedures can control the vast majority of obstetric hemorrhages if diagnosis is prompt and procrastination does not delay therapy. In a small group of cases, about one in a thousand in experience at the Mayo Clinic, however, these simple measures are ineffective owing to a pathologic process in the fundus or the lower segment of the uterus. The uterus may be ruptured, or on occasion, a true Couvelaire uterine bleeding accompanying abruptio placentae cannot be controlled by proper tamponade. Furthermore, instances of placenta previa or of leiomyomas of the uterus are encountered in which hemorrhage may be uncontrollable by vaginal procedures. Palpation on vaginal examination of the uterus and lower uterine segment usually will establish the diagnosis of uterine rupture. Abdominal exploration usually with hysterectomy is the only method which offers hope of effectively stopping these severe hemorrhages. Although the number of patients who have severe hemorrhage which cannot be controlled by simple obstetric procedures is small, they will contribute inordinately to the maternal mortality rate unless properly handled. Such patients probably would die of hemorrhage if abdominal exploration and surgical treatment are not performed, even though large volumes of blood are replaced.

Since the obstetric service was organized as a Section in the Mayo Clinic in 1922, there have been approximately 10,178 deliveries with five maternal deaths from hemorrhage, an incidence of 0.491 per 1,000 births. The first hysterectomy for obstetric hemorrhage in this series of patients was done July 3, 1935. From July 3, 1935, to May 31, 1944, inclusive, there have been 5,620 deliveries and eight patients have been treated by hysterectomy for hemorrhage. There was one maternal death from sepsis in these patients which was primarily caused by hemorrhage with a mortality of 0.178 per 1,000 births or 0.0178 per cent. This death was not one of the eight patients subjected to hysterectomy.

Report of Cases

CASE 1.—A primigravida, 31 years of age, had made twelve prenatal visits during which it was noted she had a fibroid uterus. Spontaneous

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delivery of a normal female infant weighing 3,842 Gm. occurred after an uneventful labor. Because of repeated intractable postpartum hemorrhages which could not be controlled by the usual measures employed for postpartum hemorrhage including proper uterine tamponade, subtotal hysterectomy was performed. The specimen removed included a degenerating cervical fibromyoma measuring 6 cm. in diameter.

CASE 2.—This patient had been receiving regular prenatal care at the clinic and was in the thirty-eighth week of her pregnancy when she complained of sudden rather severe pain in the right lower part of the abdomen and flank. Her only previous pregnancy had been terminated at the clinic by an elective, classical cesarean section because of a contracted pelvis.

Physical examination revealed tenderness, grade 3 on a grading basis of 1 to 4, over the right costovertebral region. Examination of a catheterized specimen of urine revealed pus, grade 4. The right ureter was then catheterized and a considerable quantity of cloudy urine was drained under pressure. This procedure relieved the patient's symptoms, so that she slept most of the night. She was observed in profound shock early the following morning. A diagnosis of intra-abdominal hemorrhage, probably from a ruptured scar of a cesarean section, was made. The shock was treated with intravenous administration of blood substitutes and whole blood so that hysterectomy could be carried out. Recovery was uneventful. It was interesting in this case to notice how completely the early signs of uterine rupture were obscured by the symptoms and findings of infection of the urinary tract.

CASE 3.—This patient, a primigravida aged 47 years, had been married three years without conception. She had made thirteen prenatal visits to the clinic since the fourth month of gestation. The pelvis was nearly normal being only slightly contracted throughout. The patient was allowed to go two weeks beyond the expected date of delivery because, although the fetus was large, it presented by the vertex and the pelvic capacity seemed to warrant a test of labor, until the last prenatal visit when the head was floating and overriding.

The patient was admitted to the hospital and an elective cesarean section was to be carried out the following morning. During the night after admission, she suddenly awoke because of vaginal bleeding and abdominal pain. The uterus was tense but the fetal heart tones were regular at 140 beats per minute. A diagnosis of abruptio placenta was made and a classical cesarean section was done at once delivering a normal male infant weighing 3,640 Gm. (8 pounds and 10 ounces) that survived.

There was some difficulty in detaching an infarcted, fibrotic portion of the placenta which measured about 2 by 2 cm. near the inferior angle of the uterine wound but no bleeding came from this part of the uterus after the placenta was removed. The uterus appeared normal on gross inspection and contracted well, so it was packed and closed in the usual manner. However, at the completion of the operation while the patient was still on the operating table, a tremendous uterine hemorrhage occurred through the pack. The vagina was tightly packed and hysterectomy was carried out at once. During much of the time consumed for these two procedures the patient was in various degrees of shock. Fluids were given intravenously in both arms simultaneously as follows: blood 3,400 c.c.; solution of dextrose 2,500 c.c.; and solution of acacia 1,000 c.c., a total of 6,900 c.c. of fluid. The concentration of hemoglobin was

15.2 Gm. per 100 c.c. before delivery, and it was 5.8 Gm. after the fluids were given. It may be calculated, therefore, that this patient lost practically her entire supply of blood by hemorrhage. Incidentally, 2,900 c.c. of blood came from group O donors while the patient was group B and yet, no agglutination phenomena occurred.

CASE 4.—A woman, aged thirty-two years, who was in her fourth pregnancy, was referred to the clinic in the third month of this pregnancy because of an anemia. The concentration of hemoglobin in the blood was 8.4 Gm. per 100 cubic centimeters. Large doses of iron were administered, but the concentration of hemoglobin was unchanged. Gastric analysis was advised but the patient did not obtain this test. At this time, some vaginal bleeding began and hospitalization was advised and refused. The patient went elsewhere, and it was learned subsequently that cesarean section had been performed because of a diagnosis of placenta previa. Tubal sterilization was said to have been effected at the time of the cesarean section.

This woman was next seen about a year and a half later when she was admitted to the obstetric service in the hospital in shock. A diagnosis of ruptured uterus from separation of the scar of a cesarean section was made and confirmed during the course of a supravaginal hysterectomy. From the history the rupture had taken place near the date of her expected delivery. It had occurred nearly twelve hours before admission, but her physician in her home locality had been called only in time to bring her directly to the hospital. The patient's convalescence was somewhat stormy, and was complicated by a rather severe psychosis developing on the twenty-fourth postoperative day. It was felt that the psychosis could have been due to cerebral damage on a circulatory basis from prolonged and profound shock.

CASE 5.—A patient, aged thirty-seven years, was admitted near term of her fourth pregnancy bleeding from what proved to be a marginal placenta previa. Rupture of the membranes alone controlled the bleeding. She was delivered of a normal infant weighing 3,800 Gm. by outlet forceps. The child survived. Because of an uncontrollable postpartum hemorrhage through a properly applied intrauterine pack, total abdominal hysterectomy was done.

CASE 6.—The patient, a primigravida aged 35 years, was referred to the clinic because of uterine pain and vaginal bleeding. From the history it was found that her systolic blood pressure had been as high as 150 mm. of mercury two years before admission, and that her systolic blood pressure had been as high as 200 mm. of mercury and had not been lower than 180 mm. in the past two months. It had been associated with albuminuria, grade 4 on a grading basis of 1 to 4. Four days prior to admission, she had had a slight episode of vaginal bleeding with irregular uterine contractions for twenty-four hours, following which she did not feel life.

On admission to the hospital the patient complained of severe, constant abdominal pain. Her blood pressure was 130 mm. systolic and 90 diastolic, the pulse rate was 100 per minute and she appeared pale and weak. Vaginal bleeding was active. A diagnosis of abruption placentae was made. The cervix barely admitted the examining finger. The patient was given 2 liters of blood and a Porro-cesarean section was performed. The uterus was extensively infiltrated by blood and was so friable that the finger could be inserted through the uterine wall without much pressure.

CASE 7.—The patient was 28 years old and in her second pregnancy. Her first pregnancy had been terminated by cesarean section eleven years previously because abruptio placentae was suspected. She was admitted at term with classic symptoms and findings of a ruptured uterus from a scar of a cesarean section. This diagnosis was confirmed when an immediate hysterectomy was performed.

CASE 8.—The patient, gravida ix, para viii, had rapid, uneventful first and second stages of labor with spontaneous delivery of a normal living infant, weighing 3,920 grams. Because of an immediate and profuse postpartum hemorrhage, the placenta was removed manually after one attempt at expression. The uterus became atonic; because hemorrhage continued, the lower segment of the uterus, cervix and vagina were firmly packed and 1,000 c.c. of blood were given. The patient's condition was good after the transfusion. About twelve hours after delivery, the packing was removed and the patient promptly went into mild shock. She did not respond to the administration of intravenous fluids and blood to a satisfactory degree and reverted into shock soon after this treatment. External vaginal bleeding was negligible. Because of the presence of shock and the fact that progressive abdominal distention and pain developed, a diagnosis of ruptured uterus was made and confirmed at the time of hysterectomy. The rent was in the lower segment of the uterus, cervix and vagina on the right side. The vaginal laceration extended nearly to the introitus. This uterine rupture must have been caused either by a somewhat too vigorous attempt to pack firmly the entire genital tract or by the violent, rapid labor which the patient had. Administration of 3,500 c.c. of blood was required to carry the patient through the period of hemorrhage and the hysterectomy. In spite of this treatment, she went into deep shock on two or three occasions, although the concentration of hemoglobin in the blood one day after operation was 10.3 grams. Interestingly enough during the period of hemorrhage, the concentration of hemoglobin was 13.6 Gm. owing to the hemoconcentration.

Comment

The age of these patients varied from 27 to 47 years with an average age of 34 years. The parity ranged from none to eight and averaged two (Table I).

TABLE I. SURVIVING CHILDREN OF THE EIGHT MOTHERS WHO UNDERWENT HYSTERECTOMY FOR OBSTETRIC HEMORRHAGE

CASE	CHILDREN LIVING	
	BEFORE LAST PREGNANCY	AFTER DELIVERY AND HYSTERECTOMY
1	0	1
2	1	1
3	0	1
4	4	4
5	3	4
6	0	0
7	1	1
8	8	9
Total	17	21
Average	2.1	2.6

The cause of the extensive hemorrhage in the eight cases was as follows: ruptured uterus in four cases; severe abruptio placenta in two

cases and intractable postpartum hemorrhage associated with placenta previa and uterine fibromyoma one case each.

Six of the eight patients received prenatal care at the clinic, and when I reviewed the records, I considered the prenatal care adequate except for one error in judgment. The patient's cooperation in this case too was open to question. In the two other instances, the prenatal care was not adequate. One of these patients did not seek medical attention throughout her pregnancy until after the uterus had ruptured near the date of her expected delivery. In the other case, gross findings of a severe hypertensive toxemia were manifest for two months before adequate treatment was instituted. In general, the severe hemorrhages suffered by these patients could not have been prevented by prenatal care alone. These hemorrhages must properly be termed sudden, serious "accidents of pregnancy." However, more vigilant and effective prenatal care might have averted three of the four fetal disasters, and avoided such severe hemorrhages as to deprive three of the patients of their uteri.

Maternal puerperal morbidity was 100 per cent as judged by the standard advised by the American Committee on Maternal Welfare. Four patients, however, did not have a rise of temperature to more than 101.2° F. The more severe febrile reactions were observed among patients who had ruptured uteri wherein large volumes of blood had been present in the peritoneal cavity. Sulfonamide therapy has been used intraperitoneally in the recent cases. Chemotherapy also has been employed orally or parenterally later in the postoperative period when indicated. There were no maternal deaths in this series.

There were four fetal deaths, or a mortality of 50 per cent. All of these deaths were prior to delivery, and in three of them, the fetus was known to have expired before admission of the mother to the hospital. Rupture of the uterus was the cause of three fetal deaths, and abruptio placenta accounted for the fourth. The fetal survival in this group of cases is improved when the babies which have been born previously by these mothers are considered. The eight women had had a total of seventeen normal surviving infants before the pregnancy under consideration, an average of 2.1 each. Including the four infants that survived the pregnancies under discussion, there was a total of twenty-one living babies, or an average of 2.6 for each mother. Only one of the eight mothers was left without a surviving infant after hysterectomy.

Shock was present in each of these cases of severe hemorrhage and in five, it was profound. In four cases blood pressure could not be elicited for a time, and in several instances positive pressure was needed to obtain a flow of intravenous fluid.

The volume of hemorrhage sustained by these women was large and often tremendous. Large volumes of blood or blood substitutes, or both, were required to keep them out of dangerous shock and to carry them

TABLE II. TYPE AND VOLUME OF FLUID REPLACEMENT GIVEN INTRAVENOUSLY

CASE	FLUIDS GIVEN INTRAVENOUSLY				BLOOD, PER CENT	HEMOGLOBIN, GM. PER 100 C.C.	
	BLOOD C.C.	BLOOD SUB- STITUTE C.C.	GLUCOSE OR SALINE SOLUTION C.C.	TOTAL C.C.		2 TO 5 DAYS POST- OPERATIVE	AVERAGE
1	500	1,000	500	2,000	25	8.0	7.1 46.0%
2	1,000	1,000	2,800	4,800	21	7.6	
3	3,400	1,000	2,500	6,900	49	5.8	
4	2,500	0	450	2,950	85	6.8	
5	3,000	0	1,000	4,000	75	7.3	9.4 60.4%
6	2,000	0	500	2,500	80	7.8	
7	2,500	0	700	3,200	78	11.2	
8	3,500	0	1,100	4,600	76	11.2	
Average	2,300	375	1,194	3,869	59	8.2	48.4%

through the hysterectomy. If the blood and blood substitutes are considered together, it will be observed that the volumes of such fluids employed varied from 1,500 c.c. to 4,400 c.c. with an average of 2,675 c.c. for each patient (Table II). Two principles have determined the amount of blood that should be administered to these patients: First enough blood should be given to secure the desired result; namely, to retrieve patients from shock or prevent its occurrence until obstetric hemostasis is attained and there is no further danger of loss of blood. Second, it is better that patients are not left with a severe anemia early in the puerperium. Barker and others¹ have shown that the risk of thrombophlebitis and fatal or nonfatal embolus after hysterectomy is more than four times as great for anemic patients as for those who are not suffering from anemia. Recently, we have tried to give enough blood so that the concentration of hemoglobin will be maintained at about 10 Gm. per 100 c.c. of blood. It is better to avoid administration of huge volumes of solutions of dextrose and saline when large volumes of blood are being given to replace fairly adequately the blood that has been lost. Solutions of saline or glucose are employed for the immediate intravenous transfusion during the few minutes that are required to obtain blood from the blood bank because they are as effective at this stage as blood and the efficiency of flow is easy to observe. From 100 to 200 c.c. of these watery solutions are administered rather rapidly and the remainder of from 500 to 1,500 c.c. is allowed to follow the blood at a slow rate. The volumes of intravenous fluids administered and the concentrations of hemoglobin in the blood after operation are shown in Table II. The cases are listed in chronologic order in this table.

Cases such as these challenge the judgment and skill of the obstetrician and test his capacity to act quickly and effectively. Instances of such severe hemorrhage are rare in general obstetric practice. However, in the small group of cases in which such severe hemorrhages

do occur, risk of death from exsanguination is exceedingly high. Because of this, such patients contribute heavily to the low maternal mortality rate in regions where the level of obstetric practice is high. In regions where the obstetric environment is less favorable, deaths from these hemorrhages also contribute noticeably to an already unfavorable maternal mortality rate. Laparotomy and repair, or removal of the uterus is the first obstetric treatment to be applied for rupture of the uterus. For other types of intractable obstetric hemorrhages laparotomy is, in a sense, a last resort but it should not be delayed too long.

The purpose of this paper is not to urge the frequent use of hysterectomy in the treatment of obstetric hemorrhage, but to point out its important place in the reduction of maternal mortality from exsanguinating hemorrhage when it is indicated. The operation is indicated when the uterus is the site of a lesion provocative of tremendous hemorrhage that is not accessible for hemostasis vaginally. Hysterectomy also is indicated when the usual methods of obstetric hemostasis, such as proper uterine tamponade through the vagina, fail. Once the indication has arisen, the operation should not be delayed, for in many instances such delay proves fatal. Removal of the uterus should be kept in mind as a lifesaving procedure for the type of patient whose cases are reported herein, and as such, it is not too radical a procedure. There is a natural reluctance to deprive any woman in the childbearing years of a normal uterus, but in the cases under discussion, the uteri were diseased and because of the lesion present, the life of the patient was acutely threatened from massive hemorrhage. Incidentally, this type of hemorrhage occurs much more commonly in multiparas than in nulliparas. In the eight cases reported, only one patient did not have a surviving child after hysterectomy and the group of eight mothers had twenty-one living children.

Summary

Eight cases of massive obstetric hemorrhage are reported that have been treated by hysterectomy. They occurred among 5,620 deliveries during a period of nine years. The fetal mortality was 50 per cent and there were no maternal deaths. Large volumes of blood and other fluids suitable for replacements were needed to sustain these patients through their hemorrhages and the operation of hysterectomy.

References

1. Barker, N. W., Nygaard, K. K., Walters, Waltman and Priestley, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism. II. Predisposing Factors, *Proc. Staff. Meet. Mayo Clinic* 16: 1-5, 1941.
2. Gordon, C. A.: Hemorrhage as the Most Important Cause of Maternal Death, *AM. J. OBST. & GYNEC.* 46: 366-373, 1943.
3. Gustafson, G. W.: Hysterectomy in Pregnancy, Labor and the Puerperium, *AM. J. OBST. & GYNEC.* 43: 221-231, 1942.
4. Hunt, A. B.: Obstetric Hemorrhage, *Minnesota Med.* 26: 355-362, 1943.

THE USE OF A NEW CONTRAST MEDIUM (VISCO-RAYOPAKE) IN THE FEMALE GENERATIVE TRACT

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THE etiologic diagnosis of continued uterine bleeding presents a challenge to the clinician. It is often very difficult to determine whether such bleeding is endocrine or mechanical in origin. Obviously, a correct diagnosis is essential to the proper therapeutic management of the patient. Strangely enough, it is sometimes easier to make a diagnosis of an endocrine dysfunction as the basis for abnormal uterine bleeding than to determine the presence of a polyp or submucosal myoma which may be responsible for the symptoms. It is a recognized fact that simple curettage of the endometrium is not reliable in ascertaining the possible presence or absence of a small polyp or fibromyoma. Furthermore, it is equally as important to determine whether or not a large, palpable fibroid extends through the uterine wall into the endometrium. Such a tumor may or may not be responsible for the patient's symptoms, depending upon its degree of infringement, if any, upon the uterine canal.

The two methods which are available to the clinician in diagnosing the presence of an intrauterine growth, or to determine whether a large subserosal fibroid is the causative factor of bleeding are: (1) direct vision, and (2) the injection of a radiopaque substance directly into the uterine canal. The direct vision method is technically difficult and objectionable in that only the operator, and perhaps an assistant or two, can visualize the interior of the organ. Furthermore, there is no easily obtainable permanent record with this method, other than the memory of the operator, inasmuch as intrauterine photography is still an experimental procedure, the cost of which is prohibitive save for research purposes.

The radiopaque substance method of visualizing the interior of the uterus is far more practicable and has numerous advantages. Rindfleisch¹ was the first to make clinical use of this method less than 35 years previously. Several years later, Rubin² and others^{3, 4} employed silver salts for this purpose. This was followed shortly thereafter by the halogens,⁵⁻⁷ which were practically replaced by iodized oils in 1922.⁸

The so-called iodized oils have been used extensively and with remarkably good results for many years, but they are not without their objectionable features. An oil, regardless of its source, has a definite tendency to become stagnant in small channels and crevices. All too frequently a foreign body reaction will occur, giving rise to strictures of the narrower portions of the female generative tract. Such constrictions

are particularly prone to occur in the uterine tubes, and if the constriction is of such a degree as to occlude the tubes completely, sterility ensues. With any degree of constriction, however, the chances for the successful implantation of the fertilized ovum are markedly lessened. Another objection to iodized oils (poppy seed oil is the medium of one of the commonly used preparations) is that absorption of the substance from the generative tract is extremely slow, and it is not rare to find by means of roentgenography sizable amounts of oil even several months or years after it was placed there.

Obviously then, these substances are not ideal for hystero-graphy. Rubin⁹ lists the prerequisites of an ideal radiopaque contrast medium as follows: (1) adequate radiopacity; (2) rapid absorbability; (3) freedom from chemical irritation; and (4) proper viscosity. One of the most recent preparations which closely approximates the ideals listed above is Visco-Rayopake.* This product may be defined as a radiopaque contrast medium containing an organic iodine compound (2,4-dioxo-3-iodo-6-methyl tetra hydropyridine acetic acid) and a polymeric form of polyvinyl alcohol. The latter substance renders the compound viscous. Rubin⁹ cites evidence to show the low toxicity of the drug. Since 3 Gm. per kg. of the contrast acid and 2 Gm. per kg. of polyvinyl alcohol given intravenously are well tolerated, the comparatively small relative amounts of the two substances (0.16 Gm. per kg. and 0.01 Gm. per kg.) received by the average patient could hardly be expected to give rise to toxic symptoms.

Methods

Visco-Rayopake may be injected directly into the uterine canal through the cervical opening, immediately following which roentgenographic studies are made, or the preparation may be introduced into a rubber bag or balloon which has previously been placed in the uterine cavity. Each of these methods has definite indications. In the small, shallow uterine cavity it is probably preferable to instill the contrast medium directly into the uterine canal through the cervix, as is common practice in the case of salpingograms. In the previously curetted uterus we prefer to insert a medium-sized de Pezzer catheter through the cervical canal with the aid of a uterine probe, then pulling the catheter down against the internal os as far as possible. Little or no leakage in the vagina occurs. This method is eminently more satisfactory than that of inserting a cannula, for it is almost impossible to prevent leaking of the medium around the instrument into the vaginal vault. We then instill the dye under low pressure until the patient complains of mild abdominal discomfort. The catheter is clamped and anteroposterior roentgenograms are taken immediately. These are followed by lateral and postero-anterior views. The latter are important in visualizing certain small polyps or submucosal myomas. As soon as the roentgenograms have been obtained, the substance is allowed to escape from the external end of the catheter. Remarkably little of the contrast medium is ever found in the uterine tubes, and the preparation rarely escapes into the abdominal cavity.

*An experimental preparation, kindly supplied through the courtesy of Dr. William T. Strauss of Hoffmann-La Roche, Inc., Nutley 16, N. J.

In those patients who have profuse bleeding and a small canal, we have found it better to perform a preliminary curettage. It is believed this procedure is necessary to prevent forcing potentially infected blood into the uterine tubes where a secondary infection may be induced.

If the uterine cavity is believed to be large, we prefer to insert a small rubber balloon into the organ and instill the Visco-Rayopake into the former. The canal is thereby well outlined, for a protruding polyp or submucosal fibroid will cause a depression of the balloon. The entire procedure is carried out under general anesthesia. Originally we found that the patient would often expel the balloon during recovery from the anesthesia, and we, therefore, attached a small de Pezzer catheter to the neck of the balloon, proceeding to introduce it as previously outlined. Six to ten c.c. of water are allowed to gravitate into the balloon before the patient leaves the operating room in order to make certain that the apparatus is in good position. The remainder of the procedure is quite similar to the no-balloon method described above.

If the patient has had rather profuse bleeding, it is customary to allow the balloon, inflated with air, to remain in situ following the taking of roentgenograms for a varying period of time. The balloon thus acts as a hemostatic agent, and is more desirable than packing the uterine cavity with gauze. Deflation and removal of the balloon can usually be performed within 24 to 72 hours.

Case Reports

To date, we have studied the generative tracts of some 20 patients having various gynecologic complaints. In every instance Visco-Rayopake has been found to outline the desired parts with clarity and sharp demarcation. There have been no reactions of any kind, and in the great majority of cases there was no roentgenologic evidence of any traces of the contrast substance in films taken about one hour after the material was allowed to drain from the internal genitalia.

So as to illustrate some of the varied type of cases to which Visco-Rayopake is applicable, we present below a few representative reports.

CASE 1.—C. J., a 26-year-old Negress, complained of severe dysmenorrhea and occasional intermenstrual spotting. For the past 2 or 3 years, despite normal menstrual period intervals and duration, she experienced distressing uterine cramps and pelvic discomfort during each entire period. The spotting was more pronounced and prevalent for the 3 months prior to examination. During menstruation the pain was most severe in the left lower abdominal quadrant, and persisted to a lesser degree for 7 to 10 days after the flow had stopped. There were no associated urinary or gastrointestinal symptoms.

Examination revealed a well-developed and well-nourished young adult Negress. The head, neck, chest and abdomen presented no abnormalities. Pelvic examination revealed a normal introitus; the vaginal mucosa was normal as was the cervix from which a small amount of blood was oozing. The uterus was in good position, and there were no masses palpated in the fornices although the left fornix was slightly tender.

Because of the pain and tenderness in the left lower quadrant in addition to the severe dysmenorrhea, the patient was advised to undergo

hysterography followed by a dilatation and curettage of the uterus. Due to the fact that the patient also had fairly frequent episodes of spotting, it was deemed advisable to insert a de Pezzer catheter prior to the Visco-Rayopake instillation in order to obtain roentgenograms from different angles which would be useful in visualizing a polyp or submucosal myoma.



Fig. 1.—X-ray of the uterine canal and Fallopian tubes after injection with Visco-Rayopake.

Therefore, under gas anesthesia the cervix was dilated and endometrial scrapings obtained for laboratory examination. Following this a medium-sized de Pezzer catheter was inserted beyond the internal os. When the patient had recovered from the effects of the anesthetic, ten c.c. of Visco-Rayopake were instilled into the uterine cavity through the catheter. Several roentgenograms taken almost immediately thereafter revealed no evidence of any polyp or submucosal myoma. However, the substance failed to enter the left tube. On the basis of this finding, an exploratory laparotomy was advised for disease in the left adnexa.

This case illustrates the manner in which Viscò-Rayopake may be used to diagnose tubal obstructions.

CASE 2.—D. L., a 30-year-old white female, complained of being unable to conceive. The family history revealed nothing of particular interest. Menses began at the age of 14, recurred every 28 days, and lasted 3 to 4 days. The past history was irrelevant.



Fig. 2.—Same as Fig. 1, in another case.

For the past five years, the patient had attempted to become pregnant. The husband presented no immediately discernible abnormalities, and the patient was referred to us for a complete gynecologic investigation.

Physical examination revealed nothing abnormal. The introitus was of the marital type, vagina and cervix were normal, and the uterus of average size in normal position. The fornices were nontender and presented no masses.

Laboratory examination of the blood and urine showed no abnormalities.

Accordingly, uterosalpingography with Visco-Rayopake was decided upon and 10 c.c. thereof instilled into the uterine cavity. Roentgenograms revealed normal outlines, the substance readily entered the uterine tubes. Ninety minutes thereafter, a hysterosalpingogram revealed no traces of Visco-Rayopake. An endometrial biopsy proved to be normal, and the patient's husband was referred to a urologist for sperm analysis.

This case illustrates how Visco-Rayopake can prove valuable in investigating the patency of the uterine tubes in a woman suspected of being sterile.

CASE 3.—C. F., a 26-year-old white married woman, complained of frequent menses with some spotting between periods. The patient had been married 8 years with no pregnancies. Menses had started at the age of 14, and had never been regular. She had had a dilatation and curettage of the uterus performed at the age of 16, but relief had been obtained for only 6 months.

During the past 3 or 4 months, the periods occurred every 14 to 21 days and lasted for 5 or 6 days. No other positive findings were elicited save for a 10-pound gain in weight in the past 18 months, and a history of considerable intolerance to cold weather.

Physical examination revealed no abnormalities of the head, chest or abdomen. The vaginal introitus and mucosa were normal. There was a considerable amount of blood flowing from the cervix, which was not eroded. The uterus was of average size, in good position and freely movable, and the fornices clear.

Laboratory examination revealed essentially normal blood and urine analyses.

In view of the distinct possibilities of an intrauterine or small submucosal polyp, it was deemed advisable to have the patient undergo hystero-graphy. Ten c.c. of Visco-Rayopake were instilled and the succeeding roentgenograms revealed some irregularity of the uterine canal, which however, was not definite enough to allow us to make an unqualified diagnosis of a polyp. None of the substance entered the uterine tubes.

A basal metabolic rate determination was reported as minus 22 per cent. Following 3 months of thyroid medication, the patient reported that she had had no uterine bleeding for one month; she was definitely improved and "felt fine."

This case is typical of the type where it is essential to know whether the bleeding is of organic or of endocrine origin.

CASE 4.—M. K., a 46-year-old woman, complained of increasing frequency of the menses associated with excessive bleeding and spotting between periods. The past history was irrelevant. Menstruation had been normal up until one year previously. There had been some weight gain, but nothing remarkable.

Physical examination revealed a normal head, chest and abdomen. The vulva, vagina and cervix presented no abnormalities. The uterus was somewhat enlarged, and multiple fibroid-like masses could be felt on the corpus. The fornices were clear.

In order to rule out the possibility of the uterine masses extending through to the mucosa and causing the profuse menstrual bleeding as well as the spotting, it was decided to instill 10 c.c. Visco-Rayopake into the uterus and then obtain hystero-graphs. This procedure revealed no irregularities, and subsequent curettings were reported as normal.

Following the administration of thyroid extract given because of a low metabolic rate, the menses became regular and menorrhagia and spotting ceased.

This is an example of a case where uterine fibroids existed in the presence of menstrual disturbances. Visco-Rayopake proved valuable in ruling out the organic lesion as the primary causative factor.



Fig. 3.—X-ray taken one hour after injection, showing rapid absorption of the dye

CASE 5.—V. P., a 32-year-old white married female, complained of lower abdominal pain of 2 years' duration. Her menses began at 14, had always been regular and lasted 4 to 5 days. For the past 2 years she had experienced dull, aching pain across the lower abdomen, more pronounced on the left, occurring during the menses, and more recently between periods as well. The pain was sometimes of such severity as to require the patient to stay in bed 2 or 3 days at a time.

Physical examination revealed no abnormalities except slight tenderness over the lower abdomen, and a partially fixed uterus with tenderness and an indefinite mass in the left fornix.

It was believed that the patient had an ovarian cyst. Prior to surgical intervention, 10 c.c. Visco-Rayopake were instilled into the body of the uterus by cannula (the patient was nulliparous and the uterine canal believed to be shallow). Hysterography showed the uterus to be pulled or pushed markedly over to the left, and the left uterine tube greatly dilated.

At operation the left tube and ovary were found closely adherent to the uterine body. The left ovary was almost completely replaced by a large cyst.

This case illustrates how Visco-Rayopake can serve as an aid in the diagnosis of disease of the uterine adnexa.

Discussion

The case reports cited here are but a few examples of the instances in which the use of hysterosalpingography is essential to the intelligent management of the patient. Heretofore, one might well hesitate to undertake such a measure because of the inherent toxicity and delayed reactions of the available products. However, with the advent of relatively nontoxic, rapidly absorbed dyes such as Visco-Rayopake, the procedure becomes more readily adaptable to routine use.

The technique which we use is simple and consists merely of the shaving and cleansing of the vulva, application of an antiseptic, followed by instillation of the medium with the patient in the lithotomy position. The entire procedure can be carried out in the x-ray room, and the patient can, in the uncomplicated cases, usually be ambulatory. In no instance did we ever note a reaction of any type from the Visco-Rayopake which was rapidly absorbed from the tissues, often within 60 minutes. In our opinion, there is no longer any place for an oily contrast medium for hysterosalpingograms.

We believe that every patient with a suspected uterine or tubal obstruction can and should be thus examined, and we foresee the day when hysterosalpingography will be a routine procedure in gynecologic examinations.

I desire to acknowledge the assistance and cooperation of Dr. B. E. Rhudy, roentgenologist, Greensboro, N. C.

References

1. Rindfleisch, J.: Berlin klin. Wehnschr. S. 780, 1910.
2. Rubin, I. C.: Surg., Gynec. & Obst. 20: 435, 1915.
3. Cary, W. H.: Am. J. Obst. 69: 462, 1914.
4. Leflorier, L.: Cited by Douay, E., J. de méd. et chir. 97: 709, 1926.
5. Rubin, I. C.: J. A. M. A. 75: 661, 1920.
6. Rubin, I. C.: Am. J. Roentgenol. 8: 120, 1921.
7. Kennedy, W. T.: Am. J. Obst. & Gynec. 3: 697, 1922.
8. Sicard, J. A., and Ferrestier, J.: Bull. et mém. Soc. méd. d. hôp. de Paris 46: 463, 1922.
9. Rubin, I. C.: New York State J. Med. 36: 1989, 1936.

ADENOACANTHOMA OF UTERUS

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ADENOACANTHOMA or squamous metaplasia, in association with adenocarcinoma of the endometrium, is a rare form of malignancy. Healy and Cutler¹ found only three out of one hundred cases of fundal carcinoma. Novak² states that the tumor is of a low degree of malignancy (Grades 1 and 2) growing slowly and metastasizing late. This opinion would not appear to be universal, however, as Meigs³ places it midway between cervical and fundal carcinoma in malignancy, and he states that metastasis is rapid and widespread.

The microscopic picture is unusual and variable. Frequently, the pattern found is that of an adenocarcinoma with islands of squamous epithelium scattered among the glands, lying free in the stroma or sometimes in the glands themselves. The origin of this ectopic squamous tissue has been the subject of much discussion. The view that it is a combination malignancy has been generally abandoned. In general, a malignant growth tends to reproduce in a disorderly embryonic fashion the pattern of the epithelium from which it arises. Novak² states that the origin is from certain "indifferent" cells beneath the normal columnar uterine epithelium, these cells possessing a differentiating potency which, under certain circumstances, can lead to the formation of squamous epithelium.

In some benign conditions, especially inflammatory lesions, squamous metaplasia may occur in the uterus, just as it occurs in the endocervix in cervical erosions. Chronic irritation in the uterine cavity might likewise cause a similar metaplasia. It is known that benign metaplasia does occur in certain cases of endometritis. Zellar⁴ has presented evidence of the effect of chemical irritants on the uterine epithelium. In 1885, he reported 63 cases of chronic endometritis showing squamous metaplasia following long-continued intrauterine application of iodine, bichloride of mercury or carbolic acid. Novak² states that he has seen no instance in which metaplastic areas revealed any indication of malignancy, though admitting that this might occur.

This tumor responds poorly to radium, and total hysterectomy and removal of the ovaries and tubes is the treatment of choice providing evidence of metastasis is not present.

Case Report

The patient was a 56-year-old female of French-Canadian extraction, who was admitted to the hospital complaining of irregular vaginal hemorrhages. When first seen in October, 1941, she had been bleeding continuously for six weeks and was suffering from weakness due to loss of blood. Her menstrual history was unusual in that at the age of 36 years, following the birth of her last child, she had a period of irregular menstruation extending over fifteen years, up to the time when the patient presented herself for examination. At times, her bleeding

would persist for several weeks continuously to be followed by periods of amenorrhea of two to three months' duration. For four months prior to her admission to the hospital, however, the bleeding had been continuous increasing at times to the proportion of a severe hemorrhage. It is of interest to note that this hemorrhagic condition accompanied an emotional upset caused by the fatal illness of her husband, and the capture and imprisonment of her son who is serving with the Royal Canadian Air Force overseas.



Fig. 1.—Showing atypical cystic glands with an island of benign-appearing squamous tissue intimately associated with the gland epithelium.

Examination revealed an obese female, who appeared anemic and weak. The blood pressure was 160/90 and the blood sugar investigation showed a latent diabetes with intermittent glycosuria. On pelvic examination, it was found that there was an almost complete upper vaginal stenosis obscuring the cervix to visual examination. This structure could be palpably defined as a small, firm, mobile organ attached to a hard, symmetrically enlarged uterus about the size of a two months' pregnancy. The uterus was quite mobile and the broad ligaments were free of palpable exudate or fixation. The adnexa could not be felt.

A laparotomy was performed, and the uterus was found to be very large and very firm, freely movable with a small cervix suspended in a mobile broad ligamentary hammock. The right adnexa appeared normal except for tubal thickening, but the left tube and ovary were only represented by a vestigial-appearing nodule the size of an olive, adherent to the round ligament and the posterior wall of the uterus. A panhysterectomy was performed, the broad ligaments and the pelvic floor being left palpably free of any glands or thickening. The patient made an uneventful recovery.

Pathologic Report.—Gross examination of the uterus revealed a fundus about the size of a baseball, uniformly symmetrical, attached to a small but elongated cervix. The uterus felt very hard and cut with

a dense leathery consistency. The uterine wall was 5 to 6 cm. thick with numerous loculi communicating with an irregularly enlarged uterine cavity. The cut section presented a uterine cavity shaped somewhat like a bunch of grapes with some of the branches extending far out into the myometrium. Surrounding each pocket the tissue appeared to be almost rock-hard, cutting only with extreme difficulty. The center of the uterine cavity showed some areas of ulceration.



Fig. 2.—Adenocarcinomatous glands and islands of malignant-appearing squamous tissue isolated in the stroma. Note extensive exudative reaction.

Microscopic examination revealed an unusual picture with many large endometrial glands presenting a hyperplastic appearance. In certain areas, however, the glands showed definite adenocarcinomatous changes (Fig. 2). Other parts showed islands of squamous epithelium, some of these presenting a benign appearance (Fig. 1); while others showed malignant changes of the squamous carcinomatous type (Fig. 2) spreading extensively throughout the endometrium. The other pelvic tissues presented nothing remarkable, and showed no evidence of metastasis.

Comment

The occurrence of two types of malignancy, the usual adenocarcinoma of the endometrium and the unusual squamous carcinoma appearing side by side in the fundus of the uterus, presents an extremely uncommon and interesting picture.

The microscopic picture presented would appear to favor stromal metaplastic origin for the ectopic squamous tissue, some islands appearing in glands while others appear isolated in the stroma away from any glandular epithelium. The finding of the epithelial pearl formation and squamous tissue showing embryonic characteristics in this case indicates that growth activity of a malignant type may occur in these squamous islands.

It would appear that we were fortunate enough to remove the pelvic organs before any metastasis had occurred. It is now three years since the operation. The patient is enjoying good health, and shows no evidence of recurrence or metastasis. Therefore, she should have a good chance of being entirely cured.

Summary

A case of adenoacanthoma of the uterus has been presented in which there is evidence of malignant change in the squamous tissue as well as in the glandular.

Brief references have been made to the literature.

The microscopic picture in this case would appear to favor stromal metaplasia as the origin of the abnormally placed squamous tissue.

References

1. Healy, W. P., and Cutler, M.: *AM. J. OBST. & GYNEC.* 19: 457, 1930.
2. Novak, E.: *Gynecologic and Obstetric Pathology*, Philadelphia, 1940, pp. 202-203, W. B. Saunders Co.
3. Meigs, J. V.: *Tumors of the Female Pelvic Organs*, New York, 1943, The Macmillan Co., p. 140.
4. Zellar, A.: *Ztschr. f. Geburtsh. u. Gynäk.* 11: 56, 1885.

CYSTIC PELVIC CHORDOMA SIMULATING AN OVARIAN CYST

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CYSTIC pelvic chordoma is a rare and interesting condition, and since it presents an additional entity in the differential diagnosis of cystic pelvic masses, we felt it worth while reporting.

Chordoma is a tumor which originates in the remnants of the notochord. According to Delafield and Prudden,¹ in man it is a transient, though important, embryologic structure which disappears early in fetal life except for traces remaining in the intervertebral discs (nucleus pulposus). The histopathologic picture is one of large vacuolated cells with smaller cytoplasm, lying in a homogeneous or finely granulated, jellylike matrix; these elements readily break down, leaving empty spaces in the intercellular material.

Chordomas may occur anywhere along the spinal cord, or develop from the sacrum and coccyx. Both benign and malignant growths have been described in the sacrum.^{2, 3}

In a very thorough and extensive review of the literature, and their personal cases, Stewart and Morin⁴ have shown that chordoma was described by Müller in 1858 for the first time; and confirmed and corroborated by Ribbert in 1894, as a distinct pathologic neoplasm. The French pathologists, too, took up the new notochord neoplasm and in 1914, Alezais and Peyron have shown and described the pathogenesis and histogenesis of the chordoma. The German literature also described cases of chordoma but none simulating an ovarian cyst. The English literature began to present cases of chordoma in the early part of 1920; and again up to 1926, Stewart and Morin reported 25 cases of chordoma in sphenoccipital area and 27 cases of sacrococcygeal region.

Rane and Riss of Paris, 1924, saw a case in the lumbar region between the fourth and fifth vertebrae. Other reports have shown cases in the lower dorsal region. Since 1858, when Müller first described chordoma and up to the present time, none of the reported cases has been so located as to present a gynecologic problem.

The morbid anatomy, according to the experiences of Stewart and Morin, varies. Clinically, the degree of mucoid degeneration present in a chordoma is an index of its comparative benignancy. The formation of mucin being in inverse ratio to the rate of cellular activity. With increasing malignancy, the tumor becomes more and more solid and opaque. One of the most striking features of the chordoma is its locally destructive effects on bone.

Chordoma is usually a tumor of low malignancy, slowly infiltrating and destructive; tends to recur after removal; exceptionally, it may metastasize.

Of the various cases reported by Stewart and Morin the age groups were as follows: -

34.9 years in the 20 cases of the spleno-occipital region.

50.6 years in the sacrocoecygeal cases; the youngest being 16 years, while the oldest was 72 years.

Males were in the ratio of 2:1.

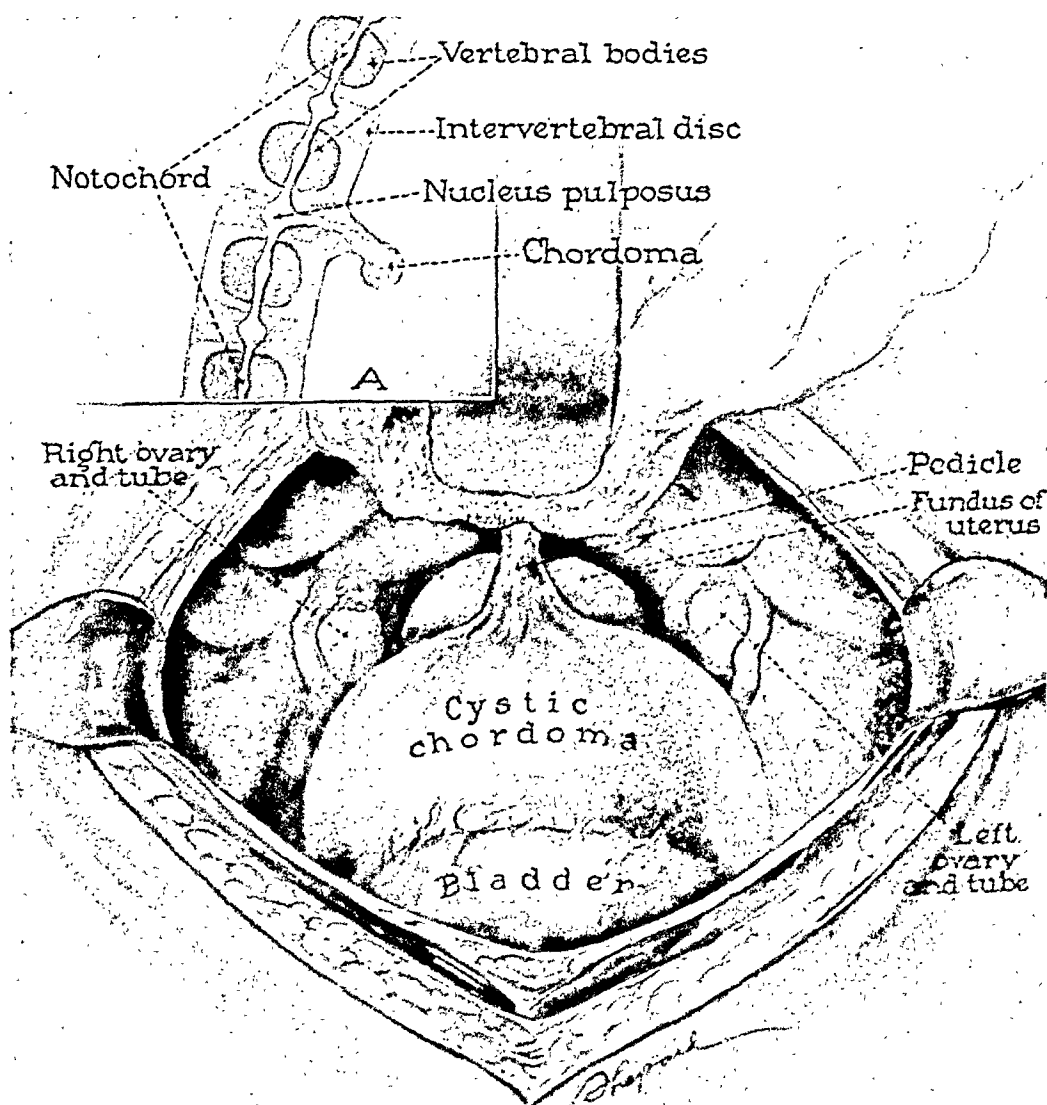


Fig. 1.—Cystic chordoma as seen during laparotomy.

Case Report

C-44-9715—D. J., aged 20 years, Negro woman, married, was admitted to the gynecologic ward of the Cook County Hospital on 3/7/44.

Complaint: Menorrhagia for 2 years. Patient stated that during her last postpartum examination in May, 1942, she was informed of the presence of a tumor on her "womb." Since the birth of her child, she noticed that her menses became "longer and heavier," using about 14 pads daily.

Began to menstruate at 15 years of age; regularly every 29 days; she had no pain with her menses.

She is gravida i, para i, and was delivered April, 1942, normally, spontaneously of a full-term baby. The remaining history is essentially negative except for hay fever for the last 5 years.

Physical examination revealed a young Negro woman who was not acutely ill. She is intelligent and cooperative. Head, neck, heart, lungs and upper abdomen failed to reveal any gross pathologic findings.



Fig. 2.—Section of cystic chordoma. ($\times 90$.)

Lower abdomen revealed the presence of a mass which was distinctly cystic, smooth, regular, and spherical, which extended up to the umbilicus. There was no rigidity, no specific areas of tenderness upon palpation. Inguinal adenopathy was absent.

Urethra, Skene's and Bartholin's glands were not diseased.

The patient was catheterized prior to pelvic examination.

Cervix was free, lacerated and pointed upward toward the symphysis.

Corpus uteri was small, firm, symmetrical and retroverted.

There was a large cystic mass which was prominently felt in the anterior aspect of the pelvis in the midline extending up to the umbilicus.

Rectally, the afore-mentioned findings were confirmed.

The impression was that of an ovarian cyst.

Laboratory findings were:

Hb. = 80%

R.B.C. = 4,100,000

W.B.C. = 8,600

Urine was negative for albumin and sugar.

Laparotomy findings: A large cystic mass measuring the size of a normal fetal head, filling the lower pelvis, was located between the bladder and uterus and was adherent to the former by an old inflammatory process. The mass was attached to a long pedicle, simulating the umbilical cord of a newborn baby, the latter passed over the mesentery to the dorsal spine. The cystic neoplasm had a thick capsule measuring approximately $\frac{1}{8}$ of an inch; it was of whitish-gray glistening hue. Many vessels coursed over this mass. When cut, sebaceous, greasy, yellowish-green substance ran out. The uterus was of normal size, firm and retrodisplaced in the cul-de-sac. Both ovaries were intact, slightly flattened and cystic, but no gross abnormalities. The tubes were congested, but free. The fimbriae were free and the tubal ostia were patent.

The mass was removed by separating it from the bladder adhesions and the pedicle was cut and transfixed as close to the lower dorsal spine as was accessible. The abdomen was closed in layers.

Pathological Report: Specimen.—Cyst had been previously opened, measuring approximately 12 cm. in diameter. Adherent to the surface are numerous fibrous adhesions. In one area on the surface are numerous 1 mm. in diameter vesicles filled with reddish fluid. The lining is green and tan covered with yellowish-white, thick purulent material. In some areas, the cyst wall is thinner and coarsely trabeculated.

Microscopic sections show areas consisting of large vesicular cells with bluish staining basophilic cytoplasm. Also present are connective tissue and many thin-walled blood vessels. Portions of tissue contain large accumulation of lymph.

Diagnosis: Chordoma, with superimposed inflammatory reaction.

This patient had an uneventful convalescence and was sent home on the eleventh postoperative day.

Summary

We present a neoplasm which originated in the lower dorsal spine, but migrated to the pelvis by virtue of a long pedicle. Its presence in the pelvis simulated an ovarian cyst.

Only by careful microscopic sections did the diagnosis of chordoma become apparent.

In going through the literature we failed to find any other case of similar pelvic location.

References

1. DeLafield, F., and Prudden, T. M.: 15th Edition, 1931, William Wood & Co., p. 413.
2. Albert, H.: *Surg., Gynec. & Obst.* 21: 766, 1915.
3. Stewart, M. J.: *Malignant Sacro-coccygeal Abdomen*, *J. Path. & Bact.* 2: 49, 1922.
4. Stewart, M. J., and Morin, J. E.: *J. Path. & Bact.* 29: 41-60, 1926.

PREGNANCY COMPLICATED BY ADDISON'S DISEASE*

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ADRENAL insufficiency in its various forms has been much discussed in literature since the initial description of the disease by Addison. Etiological factors other than tuberculosis have been recognized with a more critical analysis of pathologic changes precipitating the condition. The advent of hormonal therapy and the development of synthetic preparations have done much to prolong the lives of individuals afflicted with adrenal insufficiency.

In 1922, Gilbert Fitzpatrick¹ first reported in American medical literature a case of Addison's disease complicated by pregnancy. A careful review of all literature by him revealed eleven cases in which pregnancy and Addison's disease had coexisted. The majority of the case histories were sketchy and inconclusive, but two facts were obvious. First, that all cases died during pregnancy or shortly after delivery. Second, that the fetal prognosis was good when the pregnancy advanced to term. Fitzpatrick reported the twelfth case in which acute adrenal insufficiency developed twenty hours after delivery. The patient was treated with adrenalin and thyroid extract with survival for at least one year after the onset of the disease.

In the October 29, 1932, issue of the *Journal of the American Medical Association*, Percy A. Perkins² reported the thirteenth case of Addison's disease and pregnancy, stating in this article that no case had previously survived. There was a failure to mention the case reported by Fitzpatrick ten years previously. Perkin's case was a para-three, the third pregnancy occurring five years after the onset of Addison's disease. For one year prior to delivery, the patient had taken a cortical hormone preparation orally and she delivered normally with no post-partum complications. The author was impressed by the fact that the patient seemed subjectively improved by the pregnancy.

In the foregoing cases, the benefit of a more complete study by various chloride excretion tests was lacking. In addition, the several types of hormonal therapy more recently developed could not be evaluated. It is our purpose to report a case of pregnancy complicated by Addison's disease of fourteen months' duration, which has recently been studied in the Family Outpatient Dispensary at the Naval Hospital in Philadelphia.

The patient, a primigravida, twenty-eight years of age, reported to the Prenatal Clinic on February 4, 1944. Her last menstrual period had occurred on July 4, 1943, and her expected date of confinement was April 11, 1944. She had been ambulatory during the first seven months of pregnancy, but complained of progressive weakness and a persistent deepening of the previously existing pigmentation. She had been re-

*The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

ceiving small doses of extract of adrenal cortex hypodermically. The patient's general health had always been good and she had dated the onset, of what had been diagnosed Addison's disease, to the end of April, 1942. Three weeks previously, the patient had given blood to the Red Cross. This had been followed by marked asthenia, necessitating bed rest for three weeks, at the end of which period, the pigmentation was first noted about the face. The asthenia and pigmentation advanced quite rapidly, and it became necessary for the patient to relinquish her position as a dietitian. The pigmentation had been definitely accentuated by the pregnancy.

The husband was on active duty in the Navy and was well. The mother had died of carcinoma of the rectum. The father, one sister, and two brothers were living and well. The sister, who accompanied the patient to the clinic, was fair-complected and volunteered the information that before the initial pigmentation, their skins had been of equal fairness.

The patient was of slight build, appeared somewhat lethargic, and showed a striking bronze pigmentation of the entire body, with a deeper pigmentation of the face, hands, areolae, vulva, and thighs. The gums and hard palate were studded with accumulations of pigment that were deep brown to black. The blood pressure was 100/70. The patient was considered to have a small gynecoid pelvis, and it was felt that delivery could be completed vaginally.

Skull plates showed no bone changes, and there was no x-ray evidence of any disease process in the lungs. The heart measurements were considered normal for size and configuration. Stereoscopic plates and serial studies of the adrenal areas revealed no abnormal calcification. Ophthalmoscopic examination showed no eye-ground changes. Urinalysis was negative. Kahn and tuberculin tests were negative. There was a moderate degree of hypochromic anemia.

The patient was admitted to the hospital on February 24, for chloride excretion tests for adrenal insufficiency. The reports were as follows:

Blood plasma:	No. 1 (8 A.M., 2nd day)	584 mg. % NaCl
	No. 2 (10 A.M., 3rd day)	524 mg. % NaCl
Urine specimens:	No. 1 (8 A.M. to 8 P.M., 2nd day)	840 c.c. 330 mg. % NaCl
	No. 2 (8 P.M. to 8 A.M., 3rd day)	1,180 c.c. 240 mg. % NaCl
	No. 3 (8 A.M. to noon, 3rd day)	60 c.c. 550 mg. % NaCl

Interpretation: (According to Cutler, H. H., Powers, M. H., and Wilder, R. M., Proc. Staff Meetings, Mayo Clinic 13: 244, 1938.) If the concentration of chloride in the third-day specimen of urine is above 225 mg. per cent, Addison's disease or adrenal insufficiency is strongly suggested, and if it is less than 125 mg. per cent Addison's disease is unlikely. Plasma chloride will nearly always fall below 550 mg. per cent in Addison's disease on the third-day blood specimen.

The patient was placed on a high protein, high carbohydrate, high salt, low potassium diet and this was augmented by two grams of sodium chloride in tablet form and two c.c. of eschatin twice a day. She was given ferrous sulfate, calcium lactate, and thiamin chloride in addition to the prescribed diet. Her weight-gain had been but moderate, and she was carefully observed for any signs of fluid retention. Asthenia remained constant; the pigmentation showed a gradual deepening, and the blood pressure remained consistently low.

The first admission to the maternity floor was on April 12, 1944, at which time actual labor had not begun and the patient was discharged. She was readmitted at 5 A.M. on April 20. The membranes had ruptured five hours previously. Labor began seventeen hours later, and was terminated by an outlet forceps delivery of a normal male infant at 10:45 A.M., April 21. There was an estimated blood loss of 250 cubic centimeters. The patient was given 1,000 c.c. of normal saline before she left the delivery room.

Eschatin was continued in 5 c.c. doses twice daily, and the previous diet continued. The patient was comfortable until the third postpartum day, when there was a moderate temperature elevation, marked weakness, and nausea. Additional amounts of eschatin and sodium chloride were administered and on April 29, 500 c.c. of whole blood were given. In cross-matching, the materials were incubated for a period of one hour, no Rh- serum being available. The highest blood pressure recorded on the third postpartum day was 108/70, and the lowest on the seventh postpartum day was 76/48. Chloride excretion tests carried out on the twelfth postpartum day were unreliable because of the failure to adhere to a measured salt intake and the neglect in the administration of potassium citrate to displace the sodium radical. A single plasma chloride determination completed on the baby was 570 mg. per cent. The patient was discharged from the hospital on the sixteenth postpartum day at which time her condition was splendid.

An additional chloride excretion test was performed at the hospital on June 22, 1944, two months after delivery. The patient had been unable to obtain eschatin, and accordingly had received none for a period of two weeks. She had adhered to a high chloride, high carbohydrate, high protein, low potassium diet, and had in addition taken three grams of sodium chloride daily in tablet form. Her weight had remained constant. There had been no appreciable change in pigmentation, but there had been a rather marked general weakness. The systolic blood pressure readings during the three days of hospitalization had remained consistently below 90. The patient was placed on a fixed diet. The chloride excretion tests were as follows:

Blood specimens:	No. 1 (8 A.M., 2nd day)	562 mg. % NaCl
	No. 2 (10 A.M., 3rd day)	556 mg. % NaCl
Urine specimens:	No. 1 (8 A.M. to 8 P.M., 2nd day)	600 c.c. 500 mg. % NaCl
	No. 2 (8 P.M. to 8 A.M., 3rd day)	610 c.c. 550 mg. % NaCl
	No. 3 (8 A.M. to noon, 3rd day)	150 c.c. 720 mg. % NaCl

(The concentration of chloride in urine in the third-day specimen is stated to be more accurate in diagnosis of adrenal insufficiency than is the concentration of sodium, potassium, or chloride in serum, the concentration of potassium in the urine, or total excretion of sodium, potassium or chloride.)

We feel that this patient represents a case of chronic adrenal insufficiency. This is borne out by the presence of asthenia, hypotension and characteristic pigmentation. Gastrointestinal symptoms were not conspicuous except for frequent spells of nausea. There is no history or roentgenologic evidence of tuberculosis as the precipitating factor. The one x-ray of the heart revealed no diminution in the size of the heart shadow. The chloride excretion tests on two occasions have been con-

clusive. Pregnancy has not affected the course of the disease to date. Adrenal cortex extract (eschatin) was administered because of its availability, and the fact that the patient was subjectively improved while receiving it. It is possible that the synthetic desoxycorticosterone has its advantages because of the better standardization of the preparation.

References

1. Fitzpatrick, Gilbert: Addison's Disease Complicating Pregnancy, Surg., Gynec. & Obst. 35: 72-76, 1922.
2. Perkins, Percy A.: Addison's Disease and Pregnancy, J. A. M. A. 99: 1500, 1932.

AN. INTRAGROUP HEMOLYTIC TRANSFUSION REACTION IN AN RH-POSITIVE PATIENT

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THE cause of *intragroup* hemolytic transfusion reactions in obstetrics became of great importance following the work of Wiener and Peters^{1, 2} which implicated the Rh factor of Landsteiner and Wiener.^{3, 4} It is now considered a fact that if a pregnant woman is Rh negative and if her fetus is Rh positive, the baby's blood may sensitize the mother and stimulate the production of Rh isoantibodies. At some subsequent time, if such a sensitized woman should be given a transfusion of Rh-positive blood and if the titer of anti-Rh isoantibodies in her body should be high enough, hemolysis of the donor's Rh-positive red blood cells will take place (even though the bloods are of the same blood group), giving rise to an intragroup hemolytic transfusion reaction. The same is true of certain nonpregnant individuals who are Rh negative and are given transfusions of Rh-positive blood. The first transfusion may sensitize the recipient, so that the blood of subsequent transfusions will be hemolyzed.

However, the problem is not so simple, for the Rh factor is not a single entity, but comprises at least five distinct varieties of Rh agglutinogens which have been designated Rh₀, Rh₁ (Rh₀'), Rh₂ (Rh₀"), Rh', Rh". These give rise genetically, to the following eight Rh types: Rh₀, and Rh₁, Rh₂, Rh₁Rh₂, Rh', Rh", Rh'Rh" and Rh negative. The practical importance of this finding is that there are three principal varieties of anti-Rh sera: anti-Rh₀, anti-Rh' and anti-Rh"; and unless all bloods are tested with all three types of sera, some Rh-positive bloods may be classified as Rh negative. Moreover, in rare cases, patients of one Rh type may be sensitized against blood of a different type; e.g., an individual who is Rh' or Rh" may be sensitized by blood of types Rh₁ or Rh₂. These facts are summarized in the papers by Wiener and his associates who first described the Rh types.^{5, 6}

In addition, the subject has become even more complex since the discovery of the Hr (or St) factor,^{7, 8} which is an antigen shared by bloods of several of the Rh types, namely, Rh-negative bloods, those containing properties Rh₂, Rh₀, and Rh", and heterozygous Rh₁ and Rh' bloods; while Hr is absent from homozygous Rh₁ and Rh' bloods. The significant feature of this is that just as an Rh-negative individual may be sensitized against Rh-positive blood, so may an Hr-negative individual be sensitized against Hr-positive blood. Furthermore, an Hr-negative individual is always Rh positive. Therefore, one is not justified in feeling completely secure when transfusing an Rh-positive individual. This is seen from the case to be presented in which a transfusion reaction occurred in an Rh-positive individual, who was given Rh-negative blood, the reverse of the usual combination which causes trouble.

S. C., 26 years of age, white, gravida iv, para iii, term gestation, was admitted to the obstetrical service of Bellevue Hospital on June 2, 1944,

in active labor. Antepartum course had been uncomplicated. Her first two pregnancies, two and five years previously, ended in forceps deliveries, but were otherwise uneventful. In 1943, the patient had a normal spontaneous delivery which was complicated by a manual removal of the retained placenta and a blood loss of 850 cubic centimeters. The patient was transfused at that time with 500 c.c. of whole bank blood without any reaction.

Admission physical examination and laboratory work-up revealed nothing remarkable. After a first stage lasting 11 hours and 50 minutes and a second stage lasting 10 minutes, the patient was delivered spontaneously of an apparently normal male child weighing 5 pounds 9 ounces. The baby breathed and cried at once. The placenta remained attached to the uterus and after 1 hour and 23 minutes, it was expressed finally with a blood loss of approximately 1,400 cubic centimeters. One-third of the placenta was beefy red and did not contain normal-appearing cotyledons. The patient's blood pressure fell to 90/50 and she was given immediately 300 c.c. of plasma. Following this, her blood pressure returned to normal. About two hours after the placenta had been expressed, a transfusion of group AB apparently compatible (as determined by cross-matching) bank blood was started. This blood was only two days old. After the blood had been running 55 minutes and the patient had received almost 100 c.c., she suddenly began to vomit and had severe lumbar pain with a shaking chill. The transfusion was discontinued immediately, and an infusion of normal saline started. A sample of the patient's blood which had been taken before the transfusion was started, another sample drawn during the chill, and the donor's blood together with a sample of the baby's blood were sent to the Serological Laboratory of the Office of the Chief Medical Examiner which is under the direction of Dr. A. S. Wiener. The following were the findings:

	<i>Group</i>	<i>Rh Type</i>	<i>Hr</i>
Patient	A ₁ B	Rh ₁	Negative
Donor	A ₁ B	Rh neg.	Positive
Baby	Not done	Rh ₁ Rh ₂	Positive

Dr. Wiener's hypothesis to explain this intragroup incompatibility was that the patient had in her body anti-Hr isoantibodies which had been formed during her present pregnancy (or after her transfusion one year ago, or possibly both), having been sensitized by the Hr antigens in her baby's red blood cells. Thus, when she was transfused with Hr-positive blood hemolysis occurred. As already mentioned, the patient's blood taken during the chill showed definite hemolysis, the plasma being light orange in color.

To further test this hypothesis, Dr. Wiener performed a biologic test^{*} on the patient. The patient was given 50 c.c. of Hr-negative blood[†] intravenously and one hour later, a sample of blood was withdrawn from the patient's vein. There was no clinical reaction and the plasma taken after the test was no darker than the control plasma obtained before the injection. The patient was then given 50 c.c. of Hr-positive blood.[‡] Although the patient had no clinical reaction following this injection, a sample of blood taken from the patient's vein one hour later revealed definite though slight increase in the icteric index, and after a second hour the plasma was even darker, indicating definite hemolysis. Anti-Hr

*This blood belonged to group A₁, type Rh₁.

†This blood belonged to group A₂, type Rh₁ Rh₂.

isoagglutinins could not be demonstrated in the maternal serum, though tests were carried out periodically until one week post partum; but this absence of isoagglutinins occurs also not infrequently in Rh-negative mothers of erythroblastotic babies.

The baby was carefully observed for the possibility of developing erythroblastosis fetalis, but this did not occur. In fact, the infant's hemoglobin never dropped below 12 grams. Nevertheless, the infant was kept off the breast because of the possibility of anti-Hr isoantibodies passing out in the milk.

Summary

1. A case is reported in which the Hr factor appeared to be responsible for an intragroup hemolytic transfusion reaction.

2. The use of Rh-negative blood is not the complete answer for the prevention of intragroup hemolytic transfusion reactions.

3. The value of the biologic test in preventing dangerous transfusion reactions is reiterated.

References

1. Wiener, A. S., and Peters, H. R.: *Ann. Int. Med.* 13: 2306-2322, 1940.
2. Wiener, A. S.: *Arch. Path.* 32: 227-250, 1941.
3. Landsteiner, K., and Wiener, A. S.: *Proc. Soc. Exper. Biol. & Med.* 43: 223, 1940.
4. Landsteiner, K., and Wiener, A. S.: *J. Exper. Med.* 74: 309-320, 1941.
5. Wiener, A. S.: *Proc. Soc. Exper. Biol. & Med.* 54: 316-319, 1943.
6. Wiener, A. S., Sonn, E. B., and Belkin, R. B.: *J. Exper. Med.* 79: 235-253, 1944.
7. Levine, P.: *J. Pediat.* 23: 656-675, 1943.
8. Race, R. R., and Taylor, G. L.: *Nature (London)* 152: 300, 1943.
9. Wiener, A. S., Silverman, I. J., and Aronson, W.: *Am. J. Clin. Path.* 12: 241-248, 1942.

THORACOPAGUS TWINS—X-RAY DIAGNOSIS

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A CASE of thoracopagus twins is reported in which an antepartum diagnosis was not made. Several important features will be emphasized which, in the future, should make it possible to diagnose this condition roentgenologically during the antepartum period.

Case Report

The patient, a 26-year-old white primipara, had her last menstrual period January 2, 1942. The history, physical examination and laboratory findings were entirely negative. Her pelvis was ample. The antepartum course was normal. At about 28 weeks, the diagnosis of twins was made on physical examination. At 36 weeks, an x-ray examination definitely confirmed this diagnosis and also verified the position of the babies (Fig. 1).

Inasmuch as it was thought desirable to prolong the intrauterine life of the babies as long as possible, the patient was given 10 mg. progesterone twice weekly from the thirtieth week until delivery. She was also given 10 mg. ephynal acetate three times daily. During this period the patient had two-plus ankle edema, but no other complaints or abnormal findings.

On October 2, 1942, at 6 A.M. the patient was admitted to the hospital. The membranes had ruptured two hours earlier. The diagnosis of twins, double breech was made. Neither buttock was engaged. The cervix was dilated 2 fingerbreadths, and thin. Two fetal hearts were definitely heard, one to the right and the other to the left above the level of the umbilicus.

At 10 A.M. the cervix was dilated $2\frac{1}{2}$ fingerbreadths, and pains were strong every 5 minutes. The patient was given nembutal (gr. iii) by mouth, scopolamine (gr. $\frac{1}{200}$) subcutaneously and vitamin K (mg. 3.3) subcutaneously.

At 1 P.M. the patient had 3-minute pains. A sterile vaginal examination showed the cervix fully dilated and a double footling breech at the level of the spines. The patient was awake and rational, and was requested to bear down with her pains.

Three hours later, there was very slight descent, but no important progress. The patient was exhausted from her efforts and both fetal hearts had slowed considerably, the rate dropping from 150 to 100 beats per minute.

In view of the lack of progress and fetal distress, active intervention was decided upon. The patient was prepared and catheterized and local infiltration of the perineum with $\frac{1}{2}$ per cent procaine was completed. The baby on the right seemed to be presenting. The anterior foot was grasped and pulled out of the vagina and with it came two other feet spontaneously. The extra extremity was pushed out of the pelvis. On gentle traction of the extremities, the right baby descended so that its pelvis was just above the introitus, but it could not be extracted further. The traction forced the two lower extremities of the baby on the left to

prolapse through the vaginal opening and they could not be forced back out of the pelvis. Finally, all four legs were pulled into the vagina. The patient was given a general anesthesia and exploration of the upper vagina and uterus was attempted. This revealed a union of the babies at the umbilicus and in the region of the chest.



Fig. 1.

Several unsuccessful attempts were made to deliver these babies in the manner advocated by Williams, i.e., forcing one up and the other down and then also trying to bring both down together, forcing the head of one into the concavity of the neck of the other. The union between the babies seemed very solid and there was very little mobility.

Finally, the fetal heart sounds were lost and it was noticed that the one cord which went to both babies had ceased pulsating. A destructive operation was then decided upon after consultation with Dr. M. Goldberger.

A Jacobson hook was introduced into the uterus between the babies and pulled downward, separating them. The uterus was extremely ir-

ritable by this time and a Bandl's ring had formed which held both children firmly. After rather difficult pulling and further destruction of the babies, the right twin was delivered, and then finally the left. Both infants were eviscerated and dead. The placenta, about 8 inches in diameter, had one cord which had 6 vessels in it. It went completely as one to the babies, and apparently divided just before each group of vessels entered the umbilicus of the respective baby.

The entire procedure had taken almost an hour, but the mother's condition seemed fair after the delivery of the children. There was about 500 c.c. blood loss after the delivery of the placenta. It was deemed advisable to return the mother to her room without attempting to repair the episiotomy. She was given an intravenous infusion of 1,000 c.c., 5 per cent glucose in saline.

The mother's postpartum course was uneventful. On the fifth postpartum day, she was taken to the operating room and a secondary closure of the episiotomy was completed. Following débridement, the perineum was closed in layers, sulfanilamide powder being used in each layer. Her course was febrile for two days after the closure, but then the temperature returned to normal. The episiotomy healed by first intention. Examination on the fourteenth postpartum day was essentially negative, and the patient was discharged from the hospital.

An autopsy on the babies by Dr. Milton Halpern revealed these salient facts: The babies were twin girls, about 17 inches long, one weighing 5 pounds 2 ounces, and the other 5 pounds 4 ounces.

Because of the extensive damage to the babies at delivery, the entire picture was not clear. The babies each had an umbilicus, but there was only one sternum.

The heart of infant *A* was torn open and the pulmonary arteries branched off a single aorta of large caliber. There were two ventricles which communicated with each other, both opening into a common aorta. The abdominal contents were normal. The umbilical veins both united $1\frac{1}{2}$ inches below the notch of the liver.

The heart of baby *B* was also ruptured. This suggested the possibility that the hearts may have been joined. This heart resembled that of baby *A*. The abdominal viscera were also the same as baby *A*. No sternum was present.

Because of the mutilation, a more detailed report could not be given.

Comment

The first question to be discussed is whether the diagnosis of thoracopagus twins could have been made before delivery. The response might have been in the affirmative if the possibility of thoracopagus had been considered when the x-ray films were studied. There are several important features which were overlooked in studying the x-ray films. In almost all twins, even bi-breech, the heads are at different levels, one being higher than the other. They are not usually at almost the same level as seen here. Furthermore, the head of the right twin does not face the front of its body, but turns to the side toward the ventral aspect of the mother, and is extended. This indicates that the babies are so close together they cannot face each other. Finally, one gets the impression that the hand of the left baby is over the shoulder of the right and the arm of the right baby goes around the left, probably indicating that the babies are in the same amniotic sac (unless there is superimposition). Furthermore, the heads are in direct apposition.

Second, was cesarean section indicated if the diagnosis had been made ante partum? Also, was it indicated when the diagnosis of thoracopagus was made in this case? Many diverse opinions will be expressed in answering these questions. It has long been an obstetric rule that if one anomaly exists, there are usually others. In view of the cardiac pathology found on autopsy, these babies could not have survived. Therefore, I do not believe that cesarean section is warranted even if the diagnosis is made. If the union is merely that of skin attachment, there will be sufficient elasticity to allow the babies to deliver spontaneously. If the attachment is deeper, other anomalies are probably present. Certainly, in this particular case, the danger to the mother did not justify cesarean section.

Finally, it should be pointed out that in prolonged operative deliveries, delayed closure of the perineum is not the dangerous and unsuccessful procedure it was before the advent of sulfonamide drugs. This patient had no preoperative preparation of the wound. It was covered with a grayish membrane and had the characteristic fetid odor of saprophytic infection. Yet by simple débridement and the use of sulfanilamide in the closure, healing was prompt and complete. The expediency of delayed closure of episiotomy in cases of this type must be emphasized.

521 PARK AVENUE

UNUSUAL SEQUEL TO ATTEMPTED CRIMINAL ABORTION

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INSTANCES of perforation of the uterus by criminal abortionists are so common, that they ordinarily occasion only passing comment. I feel, however, that the following case presents several features that are sufficiently unique to warrant its being placed on record.

The patient was Miss A. V., aged 33, a short, stocky woman of Slavish extraction, who weighed 63.5 kilograms (140 pounds), and was quite obviously equipped with a heritage of unusual bodily strength and stamina. She was first seen at the Woman's Hospital of Pittsburgh on October 10, 1943. She had walked to the hospital and seemed fairly comfortable. She was complaining of abdominal pain, chiefly in the right upper and lower quadrant, and to a lesser extent, in the left upper quadrant. For a week previously, she had had pain in both lower quadrants. The pain was sharp in character, definitely not crampy, fairly severe at all times, but excruciating during and immediately following defecation. There had been no nausea or vomiting, in fact no other symptoms whatever.

Eight days before admission, she had visited a criminal abortionist, being, as she thought, $3\frac{1}{2}$ months pregnant. She was uncertain as to the date of her last menstrual period, but thought that it was about the last of June. The abortionist placed a long rubber tube in the grasp probably of a uterine dressing forceps and introduced it, as he told her, "into the womb." She felt a stab of intense pain as this was done. Gauze was packed into the vagina, and she was instructed to remove this the next day. She did this, and the end of the tube immediately protruded from the vulva. She pushed this back into the vagina and wore an ordinary sanitary pad and belt to keep it there.

She stated that the vaginal gauze removed was bloodstained and that a few drops of blood were passed during the next few hours, but none subsequently. Lower abdominal pain had begun and was fairly severe, but it was not crampy in character and there was no discharge of amniotic fluid.

During the ensuing six days, the end of the tube slipped out of the vagina several times, and was each time digitally replaced. On the seventh day, when the end of the tube came out again, she followed it up the vagina with her finger and found it extending into the cervix. In some manner, guided by the finger in the vagina, she succeeded in pushing the entire tube through the cervix. It did not come out again and she thought the pain was a little worse for a short time.

Throughout the entire seven days, she had worked every day at her usual occupation. She came to the hospital on the eighth day because her pain seemed a little worse, and because she had become alarmed by the failure of the tube and fetus to be expelled as she had been promised.

She was immediately admitted to the hospital. Her temperature was 98.8° F., pulse 82, and respiration 18. She seemed only slightly un-

comfortable. The leucocyte count was 14,600, red cells 3,740,000, and hemoglobin 77 per cent. Sedimentation rate was 18 mm. in 52 minutes. There were no abnormal findings in the catheterized urine. On physical examination, there was slight generalized abdominal tenderness, no more marked in one area than another. There was no distention, and peristalsis was normal. The fundus of the uterus was palpable, three fingerbreadths above the symphysis pubis. Fetal heart sounds were not audible. Vaginal examination revealed only the usual signs of normal pregnancy. The cervix was soft and closed. No foreign body was palpable. There was no blood, and no abnormal vaginal discharge.



Fig. 1.—Roentgenogram showing catheter in situ.

The accompanying x-ray was taken and showed a long thick rubber tube lying across the abdomen, free in the cavity. One end was sharply curved and extended upward along the cecum and reached a point apparently behind the liver. The remainder extended across the abdomen at the level of the iliac crests and roughly paralleled the course of the duodenum. (Fig. 1.)

Laparotomy was done the next day. Through a low right pararectus incision, the tube was easily found and removed. The abdominal cavity contained a moderate amount of thin and odorless, but definitely purulent fluid. A smear from this showed gram-positive cocci singly and in short chains. Culture reported four days later showed the presence of *Streptococcus viridans* and *Staphylococcus aureus*. The site of the uterine perforation was found in the midline of the uterus posteriorly just above the level of the internal os, and firmly sealed by dense adhesion of a portion of the sigmoid flexure. About this adhesion, there

was a heavy fibrinous exudate. The entire peritoneum showed the signs of active inflammation, though with very little fibrinous exudate. There were no other adhesions. The sigmoid-uterine adhesion was not disturbed. Four grams of sulfanilamide were placed in the abdominal cavity, and the peritoneum closed without drainage. An additional gram of sulfanilamide was placed in the wound and the remainder of the closure was routine. The tube removed was a small-caliber rectal tube measuring 40 cm. in length by 9 mm. in diameter.

The day after operation, the patient's highest temperature was 100° F. On the second postoperative day, the highest temperature recorded was 99.2° F., and the pulse 82. From the third day on, both pulse and temperature were normal. No sulfadruugs were given after the operation. She had no vomiting or distention, and never required catheterization. She had an enema on the fourth postoperative day, and thereafter, action of the bowels was normal. She was restored to a full diet on the fifth day after operation, allowed out of bed on the eleventh day, and discharged on the fourteenth, free from all symptoms.

The pregnancy proceeded normally until April 1, 1944. At this time, the patient suddenly developed generalized edema, hypertension, and albuminuria. She was placed on a regimen consisting of bed rest, high protein diet, sedation, restriction of fluid intake, and moderate doses of magnesium sulfate every other day. She was admitted to the Elizabeth Steele Magee Hospital on April 11, 1944. Blood pressure on admission was not unduly high, 156/92, and there was only a trace of albumin in the urine. The edema, however, was more marked than it had been, and she was complaining of headache, dizziness, and slight visual disturbances. It was feared that a disaster was impending. For this reason and because of uncertainty as to the behavior of the sigmoid-uterine adhesion during labor, a low cervical cesarean section was performed April 12. The baby was a healthy, normally developed boy weighing 3,295 grams (7 pounds, 4 ounces). From within the uterus, the site of the previous perforation could not be identified. After closure of the uterus, the sigmoid adhesion noted at the previous operation was still found to be present. There were no other adhesions, and the peritoneum appeared normal.

Recovery from this operation was uneventful. The wound healed by first intention. The edema disappeared within a week, as did all other pre-eclamptic symptoms. She was discharged on the fifteenth postoperative day symptom-free and with a blood pressure of 140/80. She was not seen again until May 26, at which time postpartum examination revealed entirely normal findings, and the blood pressure was 120/68. On June 9, the blood pressure was 122/70, and she was finally discharged, free from all complaints. The infant is developing normally.

The striking features of this case are the degree of abuse which the uterus withstood without aborting, and the tremendous resistance of the patient to infection. The pre-eclamptic toxemia might well have developed had nothing else happened.

TORSION OF APPARENTLY NORMAL OVARY, AND SPONTANEOUS AMPUTATION OF FALLOPIAN TUBE DURING ADOLESCENCE

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TORSION of the normal uterine adnexal organs during childhood, especially if accompanied by spontaneous amputation of the Fallopian tube, is a rare operative finding. Neel and Virnig¹ state that the reason for relative infrequency of ovarian tumors in childhood very likely serves as an explanation for the rarity with which twisted ovarian tumors or cysts are encountered during childhood. They cite Smith and Butler,² who state that only 25 instances of torsion of ovarian tumors before puberty were reported in the literature up until 1921. They also state that only 14 cases of torsion of the normal adnexa could be found, and of these, only 4 were under twelve years of age. Schute,³ in 1932, stated that 35 cases of torsion of the normal ovary had been reported. In the ensuing nine years, several cases have been described, mostly in the foreign literature, but from figures available, it is obvious that torsion of the normal uterine adnexa is not common. We have been unable to find any authentic report upon spontaneous amputation of the normal Fallopian tube during childhood. Barrett and Lash⁴ report a case of spontaneous amputation of the tube in a patient 40 years of age, and also cite Ries, who in 1900, described the bilateral amputation of the tubes in an adult, 32 years of age.

Case Report

The major complaint was pain in the left lower quadrant accompanied by vomiting. This patient, aged 12 years, had always been well and healthy until the day before her hospital admittance, at which time she developed a severe pain in the left lower quadrant. This continued throughout the day, and in the evening the patient vomited and remained nauseated and continued to vomit all evening. She was seen by Dr. A. G. Dow, who thought possibly she had some difficulty with the left ovary and prescribed for her. She continued to have pain and to vomit throughout the night of August 31, and was seen by the author late in the afternoon of September 1. At that time, the pain was located in both lower quadrants, although more on the left than on the right. She was also quite distended and showed considerable rectus rigidity and rebound tenderness. Nothing relieved the patient's condition and a diagnosis of an acute abdomen was made. This patient had menstruated quite regularly for one year and was due to have a regular menstrual period on September 2, 1943. Upon physical examination, she appeared anxious and had the facial appearance resembling one with peritonitis and complained of pain over the entire lower quadrant, particularly on the left. The diagnosis lay between ovary on a twisted pedicle or rupture of some hollow viscus, possibly appendiceal. Her temperature upon hospital admittance was 100.4° F.; pulse 114; respiration 30. Lab-

oratory reports: hemoglobin 81 per cent; R.B.C. 4,940,000; W.B.C. 23,100; 84 polymorphonuclear; 12 staff; 4 young; 4 baso; 6 lymph; 6 mono. Urinalysis showed a trace of albumin, 3 per cent acetone.

Recognizing the acute condition present, the patient was taken to the operating room and a midline incision was made. A retort-shaped mass was found in the cul-de-sac of Douglas, dark purple in color, the distal end about the size of a small grapefruit, pushing the uterus forward and filling the entire cul-de-sac, and because of its size and location in the hollow of the sacrum, it was difficult to deliver it out of the cul-de-sac into the abdomen. At the left cornu of the uterus, the tube was found missing and the only evidence of it was found in a stump about 1.5 centimeters in length which was well sealed off and showed no evidence of bleeding. Right tube and ovary were normal. Appendix was found to be retrocecal. The stump of the left tube was removed and the retort-shaped mass was found to be the remaining portion of the left tube containing a hematosalpinx, the fimbriated end of which had been sealed off by some process. The abdomen was closed in layers.

This patient was supported by fluids and made an uneventful recovery, and was dismissed from the hospital on the tenth postoperative day.

Pathological Report (H. E. Eggers, M.D.).—Sections of the greatly distended tube showed this to be filled with hemorrhagic material. This occurred not only in the lumen, but in the wall as well, with resultant marked distorsion. Around the vessels of the wall, there was almost uniform cuffing with infiltrated leucocytes.

Diagnosis: Hemosalpinx.

References

1. Neel, Harry B., and Virnig, Mark P.: AM. J. OBST. & GYNEC. 45: 326, 1943.
2. Smith, Richard R., and Butler, Wm. J.: AM. J. OBST. & GYNEC. 2: 507, 1921.
3. Schute, E.: Am. J. Surg. 16: 490, 1932.
4. Barrett, W., and Lash, A. F.: West. J. Surg. 51: 135, 1943.

Special Article

REPORT ON AN ENGLISH NATIONAL MATERNITY SERVICE

A Digest With Comment*

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AT THE request of the Royal College of Obstetricians and Gynecologists, a committee of English obstetricians under the chairmanship of Dr. Eardley Holland has surveyed the present practice of obstetrics in England and Wales and made certain proposals for an improved maternity program on a broad national basis. The findings and recommendations of the committee make up a forty-two page pamphlet recently issued under the title, "*Report on a National Maternity Service.*"

As may be seen from the following list, the committee members are men and women of eminence, several of whom have visited this country as honorary guests of one or another of our national societies: Eardley Holland, M.D. (Chairman), Dugald Baird, M.D., A. C. H. Bell, M.B., J. B. Blaikley, M.B., Alice Bloomfield, M.D., Francis J. Browne, M.D., Daniel Dougal, M.D., E. C. Fahmy, M.B., A. A. Gemmell, M.D., Surg.-Comdr. E. A. Gerrard, M.D., W. Gilliatt, M.S., J. P. Hedley, M. Chir., James Hendry, M.D., C. H. G. Macafee, M.B., Alan Monerieff, M.D., and James Young, M.D.

The Present Service and Its Shortcomings

Although maternal mortality rates in England and Wales have shown a gratifying diminution in recent years (from 4.49 per 1,000 live births in 1931-35 to 2.54 in 1942), the Committee believes they are still too high. It attributes the fall not so much to any improvement in the average standard of obstetric practice as to the application of new methods and drugs in the treatment of shock, hemorrhage and sepsis, and to modern technique in the investigation and prevention of bacterial infection. Thus, it points to the more prevalent use of blood and plasma transfusion, the employment of sulphonamides, the prevention of "droplet infection" by the use of face masks, the control of infection by modern barrier nursing, and the lowering of infection in hospitals by bacteriologically controlled administration and discipline. Statistics reveal that deaths from sepsis began to fall significantly in 1937, corresponding with improvements in the application of bacteriology to obstetrics and the advent of the new drugs, and deaths from other causes rather later, coinciding with the greater availability of transfusion fluids. The Committee believes also that the diminution in maternal mortality has been helped by the increase in hospitalization of maternity cases and by the better planning of their maternity services by a number of local authorities.

But the experience of the committee members as obstetrical consultants as well as two other types of evidence has convinced them that

*Prepared at the request of the Editor of the Journal.

the average standard of obstetric practice has not improved and leaves much to be desired. It is pointed out, in the first place, that the percentage of avoidable deaths remains shockingly high, ranging from 46 to 75 per cent in various reports. Secondly, the Committee notes with concern the great difference between maternal mortality rates in various parts of England. Thus, whereas this figure in 1939-1942 was 0.7 and 1.0 in Gloucester and Walsall, it was 4.2 in Oldham and South-end-on-Sea; and the opinion is expressed that this variation in maternal mortality is primarily a matter of obstetric personnel, of the individual skill of midwives, general practitioners and consultants, together with the availability of first-rate maternity institutions and equipment.

It is likewise the consensus of the report that the frequency of stillbirths, neonatal deaths and premature births is higher than it should be. Stillbirth is a problem intimately associated with the adequacy of antenatal supervision and the care given during childbirth and the puerperium. Causes of neonatal death are mainly obstetrical, premature birth being the commonest, followed closely by birth injury and infection. Prevention of these deaths is a problem for obstetrician and pediatrician in collaboration. Moreover, maternity institutions must provide modern accommodation for the newborn. In this connection the following statement is quoted: "I have been impressed by the poverty of much of the accommodation provided for the newborn baby, even in modern hospitals. There is rarely any effort to provide proper spacing of the cots. Nurses are by no means always masked, and though breast-feeding is far from universal, milk kitchens are rare. In some hospitals there is inadequate supervision of visitors to the nursery." (L. Parsons.)

But these mortality rates, although serious, are only two of the things, in the opinion of the Committee, which expose the shortcomings of the present maternity and health services. The present system has grown up in a very haphazard way so that facilities, both medical and nursing, are unevenly distributed. The deficiencies cause inconvenience, discomfort and hardship to many women at a time when things should be made easy for them. The lack of suitable maternity accommodations often makes the cost of childbirth too high, especially for parents in the middle income groups. These and other deterrents to having children lower the birth-rate.

The situation is summed up by saying that the present services are not of the class deserved by a great nation with centuries of accomplishment behind it and a great future before it. Let us give the best possible care, the report continues, to our chief national asset, the babies, and to the mothers who produce them.

Social and Economic Considerations

Although it is stressed that the primary essential for reduction of maternal mortality is sound obstetrics before, during and after birth, the Committee is not satisfied that economic and social factors can be entirely excluded. There is evidence that the mother of many children, whose income does not keep pace with the growing family, is likely to suffer from malnutrition and exhaustion. Moreover, as the social and economic order is descended from the higher ranks of business and professional men to unskilled laborers, the maternal mortality rates in any given age group show a definite rise.

In so far as stillbirth and neonatal mortality is concerned, the evidence is clear that adverse social and economic conditions materially reduce the chances of a child being born alive and materially increase the chances of its dying within one month of life. In Aberdeen, for instance, it was found that the women of a higher social class had a stillbirth rate of 11 per 1,000 total births, whereas those in the lower class had a rate of 30. "It seems probable that the primary difference lies in the health of the mothers. And health in this sense implies better feeding and more rest during the pregnancy, in addition to the better physique which results from good feeding and environment from birth." (*Report on Infant Mortality in Scotland, 1943.*)

The importance of a high standard of family life is urged in the belief that the infusing of higher moral and spiritual values into the families of a country has a profound bearing on physical and mental health. The Committee pleads in particular for the encouragement of early marriage. It believes, indeed, that measures for the extension of social security, with this end in mind, would have a sound biological foundation. Apart from the advantage of early marriage in relation to sexual morality and apart from its possible bearing on population problems, early marriage has a direct bearing on the health of mother and child. The risks associated with childbirth at a later age can always be minimized by skillful care and need never be a deterrent to marriage at any age, but nevertheless, over large groups, they do attain statistical significance. Education in sex and parenthood should be treated seriously, started young and given to both boys and girls. In connection with the employment of pregnant women, it is urged that expectant mothers be assured of protection from undue stress, physical and mental, during the last three months of pregnancy and the first six months after parturition.

The Type of Service Proposed

It is proposed that the country be divided into areas with a population of about 1,000,000 each yielding some 15,000 births a year. The maternity and infant needs of such an area would be sufficiently great to make full use of a complete service but not too large for obstetric consultants, resident within the area, to deal personally and promptly with the consultative, emergency and operative work. Naturally, the size would have to be governed by such factors as geography, density of population, size of towns, and transport. In the past, the distant or "telephone" consultant has been most unsatisfactory.

Each of these areas would have a central and supervising maternity center, ultimately responsible for the maternity and infant care of the whole region, known as a *Key or Primary Center*. Working in close association with this Key Center and under its general surveillance a number of *Divisional or Secondary Centers* would function, and under each of these certain *Local or Peripheral Centers*.

The Key or Primary Maternity Center.—This would be of such size, status and repute that it would be the consultative, teaching and research center of the area as well as the source of inspiration and leadership for all the other workers in the Service. Such a center would consist of a maternity unit of 100 or more lying-in beds with an appropriate number of antenatal and isolation beds, a department for infants, ambulance and emergency services, antenatal and postnatal

clinics, laboratories, classrooms and library. There would be an associated gynecological unit with provision for the treatment of abortions.

Such a Key Center would, whenever possible, be associated with a university and attached to a medical school, the Professor of Obstetrics and Gynecology being the Director of the teaching unit. He should be provided with a house in the hospital precincts. With him would be associated a staff of specialists, assistants of various grades, house surgeons, midwives and nurses. The infants would be in charge of a pediatrician who would be responsible for the general care and supervision of all infants. The Key Center would be the chief consultative center in the region for all types of cases, especially for unusual complications and would deal also with the ordinary institutional obstetrics of its district. There would be clinical laboratories of pathology and bacteriology. It would have a modern and well-staffed records department, and might be made the clearing-house for the records of the whole region.

The Divisional or Secondary Centers would be in large towns or in small towns in rural areas. They would not necessarily be smaller than the Key Centers, would be equipped just as well, would have a specialist staff, the senior of whom would live in the hospital and provide full range of service. Their beds would provide accommodation for their own booked cases as well as for complicated and emergency cases sent in from outside; they would provide, moreover, consultant services, both obstetric and pediatric for general practitioners.

In reading the report, one gathers the impression that these Divisional or Secondary Centers would function more or less independently of the Key Center in the management of individual cases, but would be subservient to it in respect to general policies, appointments and the like. One infers, moreover, that these Divisional Centers would be responsible to the Key Center for a high standard of practice.

The Local or Peripheral Centers would be small units in country towns and villages. They would be in charge of selected general practitioners in the district and would have a resident staff of nurse-midwives. They would have their own antenatal clinics, and would provide beds for women who wish to have institutional confinements, and for emergency cases for whom a more distant journey would be dangerous. They would be in close touch with the nearest Divisional Center, from which the specialist staff would come for consultations or operations. They would be centers for the district midwives and health visitors (presumably public health nurses), whose residential quarters might be attached. These would be the outposts of the Service, always linked with the Divisional Centers and through them with the Key Center.

Institutional Obstetrics.—Modern institutional obstetrics, the report goes on, can be made remarkably safe, and convincing statistics are cited in support of this statement. During the war the Ministry of Health has brought about an increase of 3,000 maternity beds in England and Wales so that there is now maternity accommodation in institutions for at least 50 per cent of the mothers of the country. But the Committee is firm in its belief that this is not enough and that there is a shortage and bad distribution of maternity beds for all classes of the community. It recommends providing, to begin with, for about 70 per cent of all births. The number required for a region with 15,000 births a year may be reckoned by allowing 20 patients a

year for each lying-in bed, with a proportion of antenatal beds equal to one-third of the lying-in beds. For 70 per cent of 15,000 births, on this basis, 525 lying-in beds would be needed and 175 antenatal beds, a total of 700 maternity beds to be apportioned among the various maternity centers.

Home Obstetrics.—Delivery of women in their own homes is approved provided that three conditions are observed. One is that the women are carefully selected and have had excellent antenatal supervision up to the very end of pregnancy. Another is that all primigravidae, all women who have had six children or more, all whose labors are likely to be abnormal, and all whose home conditions are unsuitable, should be excluded. The third condition to ensure safety is that home obstetrics should be supported by obstetric consultants and maternity institutions. Expert help can then be sent when required without delay or difficulty, or the patient can be moved into an institution by ambulance.

Antenatal Care.—Antenatal care must not be regarded as an end in itself, isolated from the management of labor. Pregnancy, labor and the puerperium are all of a piece and should have continuity of supervision from the same doctor or institution. Every antenatal clinic should be linked to a Maternity Center with a sufficient number of antenatal beds. The number of such antenatal beds should not be less than one-third of the lying-in beds. These are required for simple rest and observation, as well as for the treatment of complications. To take an elderly multipara, with children of all ages to look after, into a rest-bed for the last two or three weeks of pregnancy may be life-saving. A common fault in antenatal clinics is that there are too many patients per session. The consequence is that the work consists chiefly in a hunt for abnormalities and far too little time and attention are being given to the personal and educational sides (general health, rest, diet, sleep, comfort). There should be an appointment system for the patients to prevent long waits and waste of time.

Postnatal and Infant Health Clinics.—It is believed that the custom of mothers and babies attending clinics together, in the postnatal period, has much to recommend it since here the obstetrician and pediatrician can meet on common ground. However, a most critical time for the infant, as well as the mother, is the period between discharge from the hospital and the first visit to the postnatal and infant health clinic. Better continuity of supervision must be established here. Ideally the health visitor (public health nurse) should know by personal interview at the hospital or by prompt dispatch of a document, all details of the infant's feedings and should call at the mother's home on the day after the mother leaves the hospital.

Postnatal Hostels.—Many women after childbirth would be all the better for a period of recuperation or rehabilitation beyond the usual 10 to 14 days in bed at home or in a hospital. Just as an antenatal department requires to be supported with antenatal beds for pregnant women who are ill so does a postnatal department require to be supported, but in a different manner. The few weeks following the birth of a baby are a period of adjustment, especially for a young mother with her first baby. She has new worries, anxieties and responsibilities and must arrange her life to meet them. What she needs is a short period of rest and guidance, freedom from worry and household responsibilities, all the more if she is anemic or debilitated, or

has had a difficult labor or if there is trouble with lactation and the baby does not thrive. Two or more weeks in a postnatal hostel would make all the difference to the health and happiness of mother and baby. Postnatal hostels should be linked with a Maternity Center and be administratively part of the regional maternity service.

Personnel of the Service.—The chief obstetrician of a Key Maternity Center should be a clinician, a teacher and a leader. He would have great responsibilities not only in setting the standard for the whole region, but in the selection and training of young obstetricians. When possible he would have the status of a professor attached to a university. The first problem in personnel, the report continues, would be to find enough trained obstetricians and gynecologists. In the opinion of the Committee, such specialists require a postgraduate training of at least five years, the first two to be spent in acquiring more knowledge of medicine, surgery and laboratory science, and the last three in graded resident appointments in approved obstetric and gynecologic hospitals. It is one of the objects of the Royal College of Obstetricians and Gynecologists to encourage the training of specialists and to set the requisite standard and maintain it. There are, at present, in Great Britain 167 Fellows and 285 Members.

The Committee realizes that every registered medical practitioner is entitled by law to practice all branches of medicine and that it would be an interference with that right to make obstetric practice conditional on special postgraduate study and the possession of a special diploma. But it believes that he should have had special experience in this work. The Committee believes that general practitioners should take an important share in a National Maternity Service but its belief is equally strong that it is not an advantage to childbearing women that *any* practitioner should practice obstetrics and be employed in a National Maternity Service but only those with special experience. The Royal College of Obstetricians and Gynecologists grants a diploma in obstetrics to general practitioners and at present there are 332 diplomates. *The present system often places general practitioners in impossible situations. Unaided, and in unsuitable surroundings, they may have to deal with complications that would test the skill of the most eminent specialists. General practitioners and their patients should be supported and protected by a maternity service that makes provision for such situations and provides emergency transport of specialists to patients and patients to Maternity Centers.*

A remarkable feature of British obstetrics in this century is the steady rise of the midwife to a position in which she is present at about 90 per cent of the confinements and in three-quarters of these she acts as an independent practitioner with full responsibility. In 1942 there were approximately 15,000 practicing midwives on the register, about 12,250 of whom were in home practice, the remainder being employed in maternity institutions. The training of the midwife has been progressively improved and she now has to complete a course of one year if she is a state registered nurse and of two years otherwise. Midwives are conservative practitioners, aiming at natural labors, and their results are excellent.

Good as is the work done by midwives the Committee believes it could be better. They should be trained in large Maternity Centers with a first-class obstetric staff and not in a large number of petty training schools in small hospitals. Midwives should not be regarded as competent to undertake unaided the antenatal care of the expectant

mother, but should always work in collaboration with the general practitioner or the obstetrician of the clinic. When a midwife summons medical aid she usually sends for the patient's general practitioner. Better results might be expected if midwives summoned aid only from practitioners with special obstetric experience and if their work were more closely keyed into the Maternity Centers. Every midwife should be a Registered Nurse.

It is estimated that the total number of public health nurses (health visitors) engaged in maternity and child welfare work is equivalent to a whole time service of about 2,450, a number that is quite inadequate for the proper performance of home visiting. But even more important than increase of staffs is full cooperation between hospital or midwife and public health nurse. Ideally the public health nurse should call at the home the day after the mother and infant return from the hospital to help in tiding over a difficult period in which much unnecessary weaning and dietetic experiments take place.

Administration.—The whole Service should act as a single unit, with all parts integrated—maternity centers, antenatal and other clinics, obstetricians, pediatricians, general practitioners, midwives, public health nurses, etc. The Committee regards this principle of integration as absolutely essential for efficiency and feels, therefore, that it should be under a single administrative authority. It is assumed that the Minister of Health, together with competent advisors, would control such a maternity and infant health service and that it would be a component part of the general health service of the country.

Comment

This thoughtful and forward-looking survey of maternity needs in England cannot help but cause American obstetricians to ponder corresponding problems in this country. Among these problems are:

1. *What has caused the recent decline in maternal mortality?* In the United States as well as in England the maternal mortality rate has fallen dramatically over the past decade. Here, among white women, it declined between 1931 and 1941 from 60 to 27 deaths per 10,000 live births, whereas there, the diminution over the ten-year period was from 45 to 28. The Report stresses the fact that in England this fall in maternal mortality is attributable not to better standards in obstetric practice (training, skill, judgment), but to certain technical advances, notably more blood transfusion, sulfonamides and better hospital technique. Beyond question these same factors have played a most important part in the reduction of maternal mortality in the United States, but to assign them sole credit here is scarcely just. It would seem a valid assumption that the technical advances mentioned have been equally utilized in the two countries and have yielded comparable results in respect to saving of mothers' lives. Accordingly, if the reduction in maternal mortality in one of the countries greatly exceeded that in the other, the difference in all probability would be attributable to causes over and above technical advances. Now, as shown by the above figures, the decline in the maternal death rate in the United States has been greater than that in England by about one-third; and the question arises as to whether this differential may not be due to improved standards of obstetrics in this country.

It was in the decade of the thirties, let it be recalled, that numerous maternal mortality committees throughout the United States started

analyzing maternal deaths and at meetings open to the profession began discussing, in no supine language, their preventability. It was during the same decade that the American Board of Obstetrics and Gynecology was founded. At about the same time the Children's Bureau gave great impetus to public health nursing in obstetrics, so that, by 1939, 5,329 nurses, in 1,963 counties, were working in maternal and child health services and, with the help of the Bureau, State Health Departments began developing widespread teaching and consultative programs for general practitioners engaged in maternity work. Meanwhile, two great Congresses of Obstetrics and Gynecology were held where thousands of physicians and nurses received instruction and stimulation. The fact that these many agencies were established does not necessarily mean that results were achieved, but here and there evidence is continually cropping up that the efforts of these workers have not been in vain and that a substantial part of the recent reduction in our maternal mortality has been due to better obstetrics. But it should be noted as a chastening thought that we are only now catching up with the English rate.

2. *The problem of the general practitioner.* It would be no exaggeration to say that the body of knowledge which a general practitioner should have at his disposal today is twice that necessary just a few decades ago. Thus, in obstetrics he should have gained a passing acquaintance, at least, with countless new facts and techniques, from the Rh factor to x-ray pelvimetry. The increase in knowledge in other fields has possibly been even greater. To expect the average busy practitioner to assimilate and utilize all this and hence be "almost a specialist" in all fields, is wishful thinking. Yet, in isolated homes and with inadequate equipment, he is asked to attend all alone every type of obstetric case. Nineteen times out of twenty, everything terminates happily, but now and then he is faced with a complication of such gravity that the skill of the most expert obstetrician in the best equipped maternity would be taxed. This is the type of case that ultimately comes before the local maternal mortality committee and is called "preventable." It might well have been prevented had facilities been available for immediate consultation with an obstetric specialist and immediate transfer of the patient to a modern maternity hospital. "The present system often places general practitioners in impossible situations," says the Report, a statement even more true in this country than in England because a larger percentage of American women are attended by general practitioners.

The general practitioner must be supported—not in any haphazard manner as at present, not through consultation with another general practitioner—but by a pre-arranged plan which provides for immediate consultation, when necessary, with a specialist and speedy transport of the patient to a maternity hospital. State and county medical societies, as well as State and County public officials, should look into the possibility of working out such a plan.

3. *The problem of the midwife.* In the eastern section of Maryland (which is separated from the Baltimore and Washington districts by the Chesapeake Bay and is hence more or less isolated) there live a large number of Negro families, for the most part in rural areas. Expectant mothers in this group attend regularly a prenatal clinic conducted by the County Health Department and located in the county seat. There they are seen by a local practicing physician (with special obstetric training), a graduate nurse-midwife and several negro mid-

wives. The Negro midwives have had a year's training or more under the graduate nurse-midwife and at the prenatal clinic. Cases are carefully screened, primigravidae and women with any abnormality being scheduled for hospital delivery. The normal multiparae, who constitute the bulk of the clientele, call one of the negro midwives when pains begin and labor is attended by her throughout, provided no suggestion of an abnormality develops. In the latter contingency the graduate nurse-midwife is called, who in turn, after investigating the situation, reports conditions to the physician mentioned above. According to the nature of the complication, the physician may handle the case in the local hospital or refer it to one of the university hospitals in Baltimore. The Negro midwives are in private practice, so to speak, but handle only those cases which have been approved by the County Health Department, under whose surveillance they work. They receive, from the patient, \$15.00 for each confinement.

This program, worked out on a small scale to meet a local need, has functioned most satisfactorily. The patient is protected at all stages and her attendants are always supported, and through pre-arranged plan, by those with greater experience and more complete facilities.

In England, according to the Report, the majority of confinements are attended solely by midwives and with excellent results. The situation in the United States is not comparable since a rather general disapproval of midwives in this country has reduced them almost to the vanishing point. It looks now as if the pendulum may have swung too far, because it is becoming increasingly clear that well-trained and carefully supervised midwives have an important place in maternity programs for certain areas and among certain population groups where medical care is limited.

The maternal mortality rate for Negroes in the United States in 1941 was 69 per 10,000 live births or more than twice the figure for white women. About one-half of these colored mothers have no medical attendance whatsoever in pregnancy and labor. A carefully supervised midwife program would seem the best solution for this problem.

The Need for Maternity Beds.—The scandalous shortage of obstetric beds in many of our larger cities is brought poignantly to our attention by the Report's recommendation that the average hospital stay be eighteen days (twenty deliveries per bed per year). A ten-day stay is considered a luxury today in many American localities. The ratio of obstetric beds to population, as advised in the Report, seems about right and may well be noted by those responsible for maternity programs. Equally important is distribution, particularly in the more sparsely populated districts of the country. No woman in labor should be more than fifty miles from a well-equipped obstetric hospital unit with a specialist in attendance.

In sum, the Report stresses the need for a well-integrated system of maternity care. In this country also there is reason for believing that better organization of our resources in this field would yield significant results in terms of lowered maternal and fetal mortality rates.

THE LYING-IN HOSPITAL OF NEW YORK

IT WILL be difficult to give in detail within these few pages the history of an institution which covers the past 145 years. This was admirably recorded in 1938 by Dr. James A. Harrar, former chief surgeon, in his presentation of "The Story of The Lying-In Hospital." I have borrowed freely from this in presenting the history of the institution.

In 1798, through the efforts of 224 subscribers, the financial foundation for The Lying-In Hospital was established. "The very comfortable asylum for women whose circumstances will not enable them to make provision for their confinement in childbed" was opened in August, 1799. Its existence was brief for its doors were closed during the second year. In 1801, however, the use of the "square ward" of the New York Hospital was granted to The Lying-In Hospital. In that same year male medical students were permitted in the maternity ward to witness deliveries. This was the first time that such a privilege had been granted to male students in this country. Except for a brief period between June 9, 1822, and May 7, 1823, this union with The New York Hospital continued until June 10, 1827, when the Lying-In ward was permanently closed.

The Society of The Lying-In Hospital remained inactive until August, 1892, when it absorbed the Midwifery Dispensary which had been organized in 1888. The Midwifery Dispensary had been established through the efforts of Drs. James W. Markoe, Samuel Lambert, H. McM. Painter, and J. Clifton Edgar for the training of medical students in home deliveries. The 199 confinements during the first year increased to 2,583 during the third year, when it became a part of *The Society of The Lying-In Hospital*. In 1894 a suitable building to house The Lying-In Hospital was obtained in addition to the dispensary. This was the former residence of Hamilton Fish, located at Second Avenue and 17th Street. It provided accommodations for 32 patients and the necessary operating and delivery rooms and facilities for the staff of doctors and nurses. In 1902 the hospital was moved to the new eight-story building, which had been built for its use on the same site.

Until 1932 these facilities made possible the teaching of thousands of undergraduate and graduate physicians. The teaching in the medical schools at that time was limited to didactic and clinical lectures. The large outdoor service, therefore, provided the only means whereby the students, under the supervision of the house staff and attending surgeons, came in actual contact with patients. They not only performed the deliveries and witnessed and assisted at operations, but also gave anesthetics and the necessary postpartum care. In some years as many as 3,000 cases were handled on the outdoor service, thus providing a satisfactory insight into obstetric practice to many prospective young physicians. The district covered by the service extended from the Battery to 42nd Street, the antenatal care being rendered in two clinics; one at the main hospital and the other on Broome Street on the lower east side. Abnormal cases were transferred by ambulance from the home to the hospital. The good results obtained were evidenced as

early as 1918 when the hospital was able to report the maternal mortalities in their first 69,071 consecutive tenement house confinements as 218, one in every 317 labors, or 3.156 per thousand births. These statistics

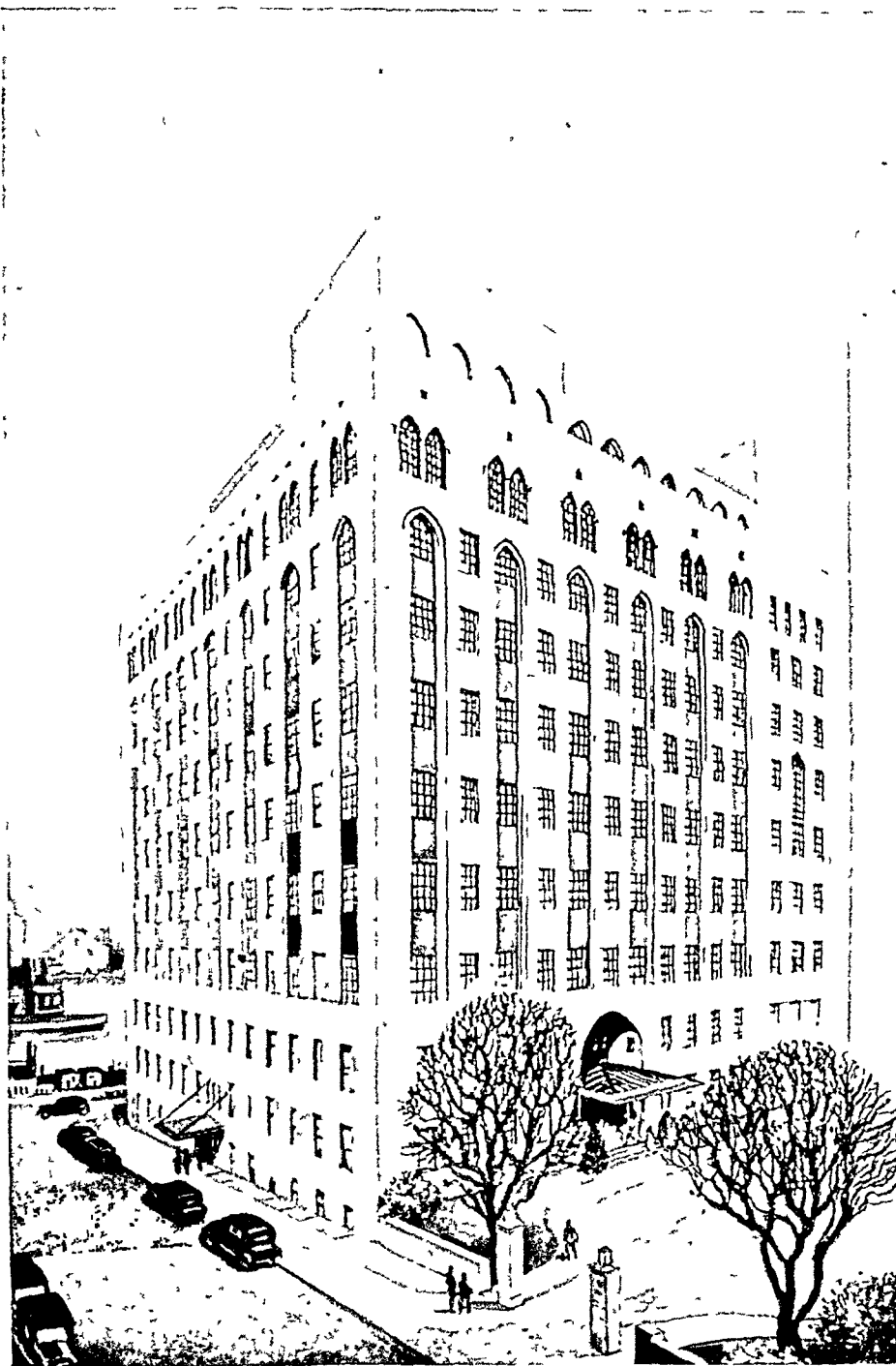


Fig. 1.—The new Lying-In Hospital—September, 1932.

are uncorrected and include all cases transferred during labor or post-partum into the Lying-In or other hospitals and dying there.

The teaching of students and physicians was not limited to the outdoor service. An average of 43 house officers, 101 undergraduate stu-

dents, and 51 postgraduate students were graduated every year. In the thirty-year period between 1902 and 1932, over 5,800 doctors were given a brief bedside instruction and experience in actual deliveries. The 200,270 babies delivered since 1890, indoor and outdoor service combined, offered ample opportunities for the training of these men.

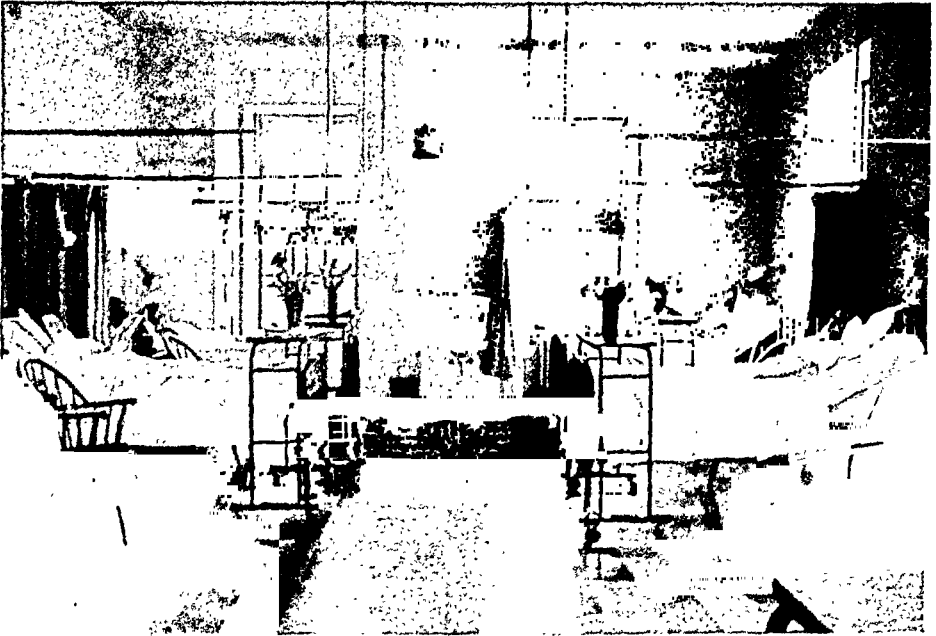


Fig. 2.—Photograph showing a typical four-bed ward.



Fig. 3.—Photograph of a typical delivery room.

The Lying-In Hospital likewise contributed greatly to the field of research. It established one of the first obstetric pathology laboratories in the country. The hospital pioneered in research on relief of pain during labor which culminated in the use of morphine and scopolamine

hypodermically, followed by the rectal instillation of ether in oil. This method was based on the original work of Dr. James Gwathmey, the anesthetist at the hospital.

In 1904 the *Bulletin of the Lying-In Hospital* made its first appearance as a scientific publication. The Bulletin appeared at intervals until 1932 when it was discontinued.

The Lying-In Hospital remained a separate institution until 1928 when it again became a part of The New York Hospital after a lapse of 101 years. This was made possible through the generosity of four individuals who subscribed the \$6,000,000 necessary for the merger. At that time The New York Hospital, with Cornell University Medical College, was contemplating new buildings for their joint enterprise.

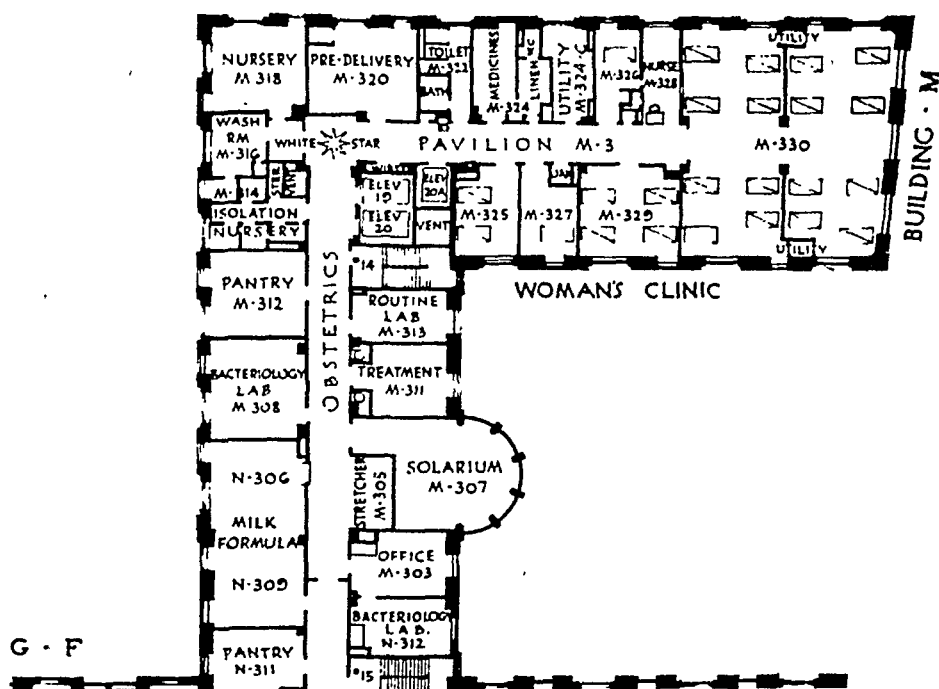


Fig. 4.—Floor plan of a typical obstetrical ward.

The present Lying-In Hospital or the *Woman's Clinic of The New York Hospital* is part of the 1,000-bed medical center located between 68th and 71st Streets from York Avenue to the East River. The eleven-story building housing The Lying-In Hospital has complete facilities for teaching and research in addition to outpatient service and accommodations for 192 patients. With the new affiliation The Lying-In became a combined Obstetrical and Gynecological Clinic. Of the total number of beds, 26 rooms are available for private patients and 36 beds for semiprivate patients. Of the 130 ward beds, 40 are devoted exclusively to gynecology. Isolation cases are cared for on one floor devoted entirely to this purpose. In itself and as part of the medical center it presents every opportunity for the teaching of medical students and house staff and for investigative work in all the branches of its specialties.

The medical staff, under the direction of Dr. H. J. Stander, obstetrician and gynecologist in chief and professor of obstetrics and gynecology, is composed of both full- and part-time physicians. No courtesy staff

is maintained. Each member of the staff shares in the teaching of students and in the supervision of the care of ward patients. The full-time staff devotes all of its time to teaching, research, and the care of patients.

The prewar schedule called for a house staff of 18 members. Six interns are appointed each year for a period of two years. At the end of the second year two interns are selected to complete the residency of five years. With each succeeding year of training the house staff assumes greater responsibility so that during the final year (fifth year) the residents are directly responsible for the care of the ward patients. Throughout the period of training the schedule is arranged to permit equal distribution of work between obstetrics and gynecology, and ample opportunity is afforded for original investigative work. The house staff assists the attending staff in the care of their private and semiprivate patients. The home delivery service was discontinued in 1942. By special arrangement the Pediatric Department of The New York Hospital cares for the premature babies born in The Lying-In Hospital and is consulted whenever indicated in the care of the newborn infant in the nurseries. This offers an excellent opportunity for the house staff to study the problems associated with the care of the newborn infant.

With the exception of serology and postmortem examinations, all the necessary examinations, including bacteriology, chemistry, pathology, and x-ray are performed at The Lying-In Hospital. This arrangement permits the utilization of such facilities for investigative work of all types. House staff participation in these departments is encouraged as a basis for the sound practice of obstetrics and gynecology.

The eighth floor of the building is devoted entirely to delivery rooms, operating rooms, and labor rooms. Two operating rooms are used for gynecological operations. The senior medical students devote two months to work in obstetrics and gynecology, and during this period they are housed within the building so that they may observe and assist with major complications whenever they occur.

The lower floor is devoted to the outpatient service. In addition to the routine obstetrical and gynecological clinics, specialty clinics are conducted. These include cardiac, toxemia, postpartum, cystoscopy, sterility, endocrine, radiation, etc.

Special staff conferences are held each Monday and staff rounds each Friday. Journal Club meetings are held monthly.

Since the opening of the new building in 1932 (Sept. 1, 1932-Dec. 31, 1943), The Lying-In Hospital has cared for 46,861 obstetrical patients and 12,262 gynecological patients. The yearly averages are 3,300 deliveries and 1,100 operations. The data of all these cases are available for study on the special punch card system which has been maintained since 1932.

John B. Pastore, M.D.

New York, N. Y.

Department of Reviews and Abstracts

Selected Abstracts

Extrauterine Pregnancy

Alvarez, Cesar Sotolongo and Boullon, Roberto Curiel: *Interstitial Tubal Pregnancy*, Bol. Mens. Hosp. Policia Nacion. 3: 49-60, 1944.

The authors describe two cases in which the left tube was involved and ruptured during the third month of pregnancy. An atypical hysterectomy of the fundus with removal of the tube was performed in one case, and a subtotal hysterectomy with removal of the tube in the other case. Recovery was uneventful.

The authors emphasize the following points: Blood transfusion must be performed, whenever possible, before beginning the operation, to combat shock and avoid starting the anesthesia during shock, as this constitutes a grave risk for the patient. In severe hemorrhage there is no marked transition between the state of peritoneal shock and the picture of internal continuous hemorrhage, and one should not wait too long in the hope that the gravity of the condition is due entirely to shock; instead, a transfusion should be given, stimulants administered and the patient operated upon immediately, because the condition will not improve until the bleeding artery is ligated. When it is ligated, the pulse and the arterial pressure will rise gradually, and the stimulants will be of real usefulness.

The operation for ectopic pregnancy must be strictly conservative and excision limited to the organ involved by the ovular nidation. The intervention must be rapid and simple under general anesthesia; spinal anesthesia is advisable only for cases operated upon before rupture occurs and having an arterial pressure appropriate to this type of anesthesia.

J. P. GREENHILL.

Decoppet, H. F.: *The Treatment of Essential Dysmenorrhea*, Schweiz. med. Wchnschr. 74: 329, 1944.

In a series of 22 cases of essential dysmenorrhea, Decoppet of Lausanne made a diagnosis of hyperthyroidism in 90 per cent. He based his diagnosis on finding a B.M.R. of more than 20 per cent in 6 cases, a B.M.R. of more than 15 per cent in 5 cases, and a B.M.R. between 10 and 15 per cent in 9 cases. He attributed the dysmenorrhea in these 20 women to the hyperthyroidism, and the *modus operandi* was a deleterious action of thyroxin on the ovaries, by producing congestion of the ovaries at the time of menstruation. The thyroid hormone which is antagonistic to thyroxin is diiodotyrosin. The latter lowers the basal metabolic rate.

In the 20 cases of essential dysmenorrhea, the author used diiodotyrosin and secured relief in 75 per cent of the cases. The amount and duration of the flow were not influenced by the medication.

J. P. GREENHILL.

Gynecology

Da Costa, C. C.: Lymphogranulomatous Parametritis and Pelvic Cellulitis, *Obst. y ginec. latino-am.* 2: 37-43, 1944.

Lymphogranulomatosis has become a fairly common disease in Rio de Janeiro especially among the lower classes, and hence, has become an important gynecologic problem. Da Costa along with H. Duck examined 1,279 prostitutes and found a positive Frei test in 41 per cent of them. In the early stages the sulfonamides may be helpful, but in the late stages when chronic edema, extensive ulceration, anorectal stenosis, etc., are present, treatment can only be palliative.

Two interesting observations were made, namely, relaxation of the anal sphincter and granulomatous parametritis and pelvic cellulitis. The anal relaxation is associated with fissures, ulcerations, stenosis, etc., and is probably due to an inflammation of the anal nerves followed by paralysis and loss of tonicity of the sphincter. The involvement of the parametrium and the pelvic cellular tissue is due to centripetal spread of the infection.

J. P. GREENHILL.

Chamberlin, George W., and Payne, Franklin L.: Urinary Tract Changes With Benign Pelvic Tumors, *Radiology* 42: 117, 1944.

The authors studied 96 patients with benign pelvic tumors with reference to excretory urography before and after removal of the tumors. Obstruction and displacement or both were present in 66 patients. The position of the tumor was more important than the size. Intraligamentous tumors produced the highest evidence of alterations in the urinary tract. All of the above changes disappeared completely following removal of the tumors.

WILLIAM BERMAN.

Fluhman, C. F.: Clinical Use of Extracts From the Ovaries, *J. A. M. A.* 125: 1, 1944.

The author describes the various preparations of estrogens and corpus luteum products and mentions the indications for their use. The potencies of the preparations and the suggested dosages are also mentioned. Great stress is laid upon the abuse of these hormones. An interesting chart of the various commercial preparations of estrogenic substances is included.

WILLIAM BERMAN.

Stegeman, W.: Incarcerated Pelvic Kidney Exhibiting Unusual Features, *Am. J. Surg.* 55: 156, 1942.

A case of pelvic kidney is reported in a 26-year-old female who complained of pain in the right lower quadrant of the abdomen. At operation, a small kidney was found the upper pole of which was incarcerated due to pressure from the encircling large renal vessels. Rotation of the kidney so that the pelvis was displaced forward and the lower pole anteriorly and laterally also resulted. Attempts at freeing the incarceration were unsuccessful due to uncontrollable bleeding, and this necessitated nephrectomy. The author believes that the patient's pain was due to the pull of the renal vessels which also produced compression and rotation of the kidney.

FRANK SPIELMAN.

Labor, Physiology, Management, Complications

Beruti, Josué A.: *Birth of the Argentine Quintuplets, Semana méd.* 51: 689-697, 1944.

The author has reconstructed the event from the data furnished by the parents, Franco and Ana Diligenti, and by the midwife, Angela Delfino, who attended the birth with the help of her niece. The data obtained must be regarded as reliable because the parents and midwife are intelligent persons who gave clear and precise answers to the questions, without any reserve.

Ana A. de Diligenti, Italian, 35, with normal antecedents, has a son, 14, from a former union and a son, 7, of her present union. Five and a half years ago, she had a triplet abortion of two and a half months.

The last menstruation occurred at the beginning of October, 1942; birth was expected about the middle of July, 1943. The pregnancy was uneventful.

During the morning of July 14, the patient developed slight, irregular pains and was admitted to the residence of the midwife.

At 7 P.M., examination revealed an extremely tense abdomen, many fetal parts, fetal heart tones all over. The diagnosis made at seven months of twin pregnancy was confirmed.

At 9 P.M. the pains disappeared until midnight, during which time the patient slumbered. On July 15, at 1 A.M. there was a slight loss of mucus and blood; contractions reappeared with increasing intensity.

At 7 A.M. the patient went to the bathroom and spontaneous rupture of the membranes occurred. Dilatation was complete. At 8 A.M. a subcutaneous injection of 1 c.c. of pituitrin was given and at 9 A.M. Carlos in vertex presentation was born. At 9:10 A.M. spontaneous rupture of a second sac occurred and the birth of Franco in vertex presentation took place. At 9:25 A.M. Maria Cristina was born as an incomplete breech presentation with manual aid (arms brought down).

At 9:45 A.M. there occurred spontaneous expulsion of a placenta weighing about 700 grams. There was slight loss of blood and the patient felt faint. The midwife wanted to call a physician, but the patient objected strenuously.

At 10:15 A.M. spontaneous rupture of another sac took place with escape of a large quantity of amniotic fluid. Immediate birth of Fernanda in vertex presentation followed. At 11 A.M. there was spontaneous rupture of another sac with the birth of Maria Esther as an incomplete breech presentation with manual aid. The child was markedly asphyxiated but was resuscitated by clearing the respiratory tract, cutaneous stimulation, hot bath, artificial respiration, and injection of lobeline.

At 11:15 A.M. there was great loss of blood, controlled by massage of uterus. At 11:25 A.M. there was spontaneous expulsion of a second placenta of about the same volume and weight as the first.

The total loss of blood was estimated at from 800 to 1,000 Gm., and the total amniotic fluid at from 400 to 500 grams.

On the fifth day post partum, the patient was taken home with three of the children. The two weakest ones were left in care of the midwife for four months. The puerperium was normal and afebrile with the exception of the day of the delivery; in the afternoon, the temperature rose to 38 C., but fell to normal in the evening.

After birth, each child was immediately wrapped in cotton wool and kept warm with stove heat and hot-water bags. Incubator, oxygen and carbon dioxide were never used. Baths were forbidden for the first three months.

The weights of the babies after 24 hours were in order of birth: 1,300, 1,200, 1,150, 1,500 and 1,250 grams. From the beginning the babies showed great vitality and had a pink skin without lanugo or vernix caseosa. According to the midwife, they were not premature babies. All are living and well.

J. P. GREENHILL.

Torres, J. I.: Version by Purgation and Enema in Podalic and Transverse Presentations, *Rev. de ginec. y d'obst.* 3: 115-123, 1943.

The author reports results in 50 cases. Castor oil (30 Gm.) is administered at night, with an enema the following morning. Version was accomplished successfully by this means in 37 cases. In seven, version was not achieved, but was facilitated by purgation and enema. In six instances, this measure failed to produce version.

The author concludes that version by purgation and enema is easy to produce and carries no risk either for mother or fetus. He believes that in every pregnancy of more than seven months, in which there is breech or transverse presentation, this procedure should be used. In case of failure, version by external manipulation should be attempted, taking advantage of the evacuation of the intestines. This can be done without additional preparation of the patient.

J. P. GREENHILL.

Newborn

Paz Silva, Haroldo: Fetal Gigantism at the Maternity Concepcion Palacios, *Rev. de ginec. e d'obst.* 3: 157-188, 1943.

Accepting 4,500 Gm. as the lowest weight for giant fetuses, the author finds that their incidence in Venezuela is low when compared with other statistics. The highest weight registered at the maternity was 5,100 grams.

The so-called physiologic causes of gigantism were confirmed by the present study, but little can be said about the pathologic causes.

As is usually the case everywhere, the diagnosis of giant fetus was made only at birth and in many cases later. The course of pregnancy was not altered by the presence of a giant fetus. The incidence of breech presentation was 7.69 per cent.

Comparison of the percentage of complications and interventions during labor given by other authors shows that the birth of giant fetuses in Venezuelan women is much less harmful. However, there was a high rate of maternal morbidity which reached 50 per cent.

Taking into consideration the accepted weight of 4,500 Gm., the infant mortality is relatively low, especially when compared with that given by Karl Wilson (20 per cent) and by Zangemeister.

From the results obtained, the authors conclude that spontaneous delivery may be expected in a large percentage of Venezuelan women.

J. P. GREENHILL.

Sorsby, Arnold, and Hoffa, Elizabeth L.: The Sulfonamides in Ophthalmia Neonatorum, *Brit. M. J.* 4340: 353, 1944.

The authors found that in the treatment of ophthalmia neonatorum, there was no appreciable difference in the action of the four sulfonamides. Sulfapyridine because of its greater toxicity appears to be the least desirable of these sulfonamides. Gonococcal cases responded more rapidly to sulfonamide therapy than did the non-gonococcal cases. The gonococcal cases showed a 51.7 per cent clinical cure within

3 days against 23.2 per cent of the nongonococcal cases. Delay in starting sulfonamide therapy did not affect its efficacy. All cases of corneal ulcer cleared after treatment.

WILLIAM BERMAN.

Pregnancy, Physiology, Diagnosis

Sisco, R. Dominguez, and Agüero, Oscar: Early Signs of Pregnancy Revealed by Genital Examination, *Rev. de ginec. e d'obst.* 3: 189-197, 1943.

The authors state that the signs found on inspection are those of Jacquemier or Chadwick (cyanosis of the genital mucosas), Kluge (varicosities of the vulva), and Berstine and Montgomery (marked swelling and redness of the orifices of the urethra and Skene's glands).

Digital examination through the vagina or rectum, alone or combined with abdominal palpation, reveals signs belonging to the vagina, cervix, uterine body and adnexa.

The vagina provides the signs of Osiander (increase in the beats of the uterine artery) and Sanger (possibility of feeling the ureters through the posterior vaginal wall).

The cervix gives the signs of Goodall (softening), Sellheim (rounded form of the lower portion) and DeLee (presence of two softened strips parallel to the length of the cervix).

The uterine body, including the isthmus, presents the signs of Hegar (softening of the isthmus giving the impression that the two examining fingers practically touch one another), MacDonald (mobility as if the uterine body and the isthmus were hinged), and Gauss (lateral movement of uterus not transmitted to the cervix).

The difference in consistency between the pregnant and nonpregnant uterus gives the signs of Bonnaire (feeling of ripe fig), Braun-Fernwald (different consistency of the two halves of the uterus), Ladin (above the cervix, a soft spot the size of a small coin which increases gradually as pregnancy advances), Runge (possibility of making a small depression on the anterior surface of the uterus by pressure of the finger through the vaginal wall), and Rasch (peculiar elasticity of the pregnant uterus).

The changes in the form of the uterus have served as a basis for the description of the signs of Piskacek (marked protrusion of one of the horns), Dickinson (marked enlargement of the anteroposterior diameter which becomes greater than the transverse; may be one of the earliest signs), Noble or Noble-Budin (resistance of vaginal cul-de-sacs due to enlargement of lower portion of uterus) and Metzger (bulging of anterior cul-de-sac).

Other signs provided by the uterus are those of Braxton-Hicks (first sign: intermittent contractions beginning from the eighth week of pregnancy; second sign: fetal dance), Bucura (decrease in size by contractions) and Loenne (fluctuation of amniotic fluid).

The adnexa present the sign of Freund and Eupinger (poor mobility and pain on pressure of the ovary which contains the corpus luteum of the pregnancy).

Nowadays many of these signs have only a historical interest and their investigation is doubtful and not without danger in many cases. But it is also true that all means must be used to reach a positive diagnosis without jeopardizing the interests of mother and fetus. The investigation of the signs of Goodall, Noble, Piskacek, Hegar, etc., together with other manifestations outside the genitalia, must lead to the correct diagnosis in most cases; but when there is doubt, and knowledge of the presence of pregnancy is imperative, recourse must be taken to the biologic tests which are about 100 per cent reliable.

J. P. GREENHILL.

Correspondence

Placental Changes in Toxemia of Pregnancy

To the Editor:

It was gratifying to note that in their excellent article Jack H. Hill and Wm. K. Trimble (Placental Infarction as a Diagnostic Criterion of Maternal Toxemia, AM. J. OBST. & GYNEC. 48: 622, Nov., 1944) reported that they could find no placental changes characteristic of so-called toxemias of pregnancy. This is in close accord with our report (Siddall, R. S., and Hartman, F. W.: Infarcts of the Placenta: A Study of Seven Hundred Consecutive Placentas, AM. J. OBST. & GYNEC. 12: 683, Nov., 1926). Examinations of thousands of placentas since our publication has convinced me of the essential correctness of our original observations. Infarction of every kind is likely to be greater with the toxemias (though not necessarily present at all), but in agreement with Hill and Trimble I have been unable to identify certain other placental changes confidently described by some as peculiar to toxemia.

Of interest in another respect was the nearly identical incidence of toxemia in their cases and ours (6.5 and 6.4 per cent), using essentially the same criteria. I strongly suspect, however, that even these comparatively low figures fail to give the true picture. It is to be noted that they are derived from hospital series and therefore presumably include a number of patients who would have been delivered normally elsewhere but were sent to the hospital because of the toxemia. My associate, Dr. Harold C. Mack, and I found that less than 4 per cent of the obstetric patients regularly under our care developed toxemia, and this figure is confirmed by that of 4.4 per cent at Harper Hospital, where there is a very low rate of emergency obstetric admissions (Siddall, R. S., and Mack, H. C.: Weight Changes and Toxemia of Late Pregnancy, AM. J. OBST. & GYNEC. 36: 380, Sept., 1938). The true incidence of toxemia, then, is probably considerably lower than usually estimated on the basis of hospital statistics. This point is important when, for instance, a possible preventive of toxemia is being tried out in consecutive cases. Incidentally, though readily granting the value and advantages of prenatal observation in discovering toxemia early, I am not convinced that any measures so far suggested are efficacious in actually preventing its onset. There are bits of evidence suggesting that some may even be injurious. Possibly to be included in this group is the present popular one of strenuously trying to prevent water retention, since it is to be remembered, for example, that in the hot months when some degree of demonstrable edema is found in nearly every woman late in pregnancy, toxemia is least common. And, one might cite the fact that eclampsia with associated edema is generally less severe than the "dry" type.

ROGER S. SIDDALL, M.D.

DETROIT, MICH.
DEC. 14, 1944.

Benefit From Early Clamping of Umbilical Arteries

To the Editor:

In any part of the body from which the arterial blood flow has been completely interrupted further, movement of venous blood is dependent upon negative pressure. A compression or milking of that area rapidly produces empty veins

and a bloodless area. It has been my belief that the application of this knowledge in the treatment of the umbilical cord should result beneficially to the newborn infant.

Recent literature has emphasized the importance of delayed clamping of the cord,^{1,2} one writer's work suggesting that there is even an increase in the infant's blood volume during the period of placental expulsion.²

During the past several months I have been attempting to improve on the above-mentioned method of delayed clamping of the cord by an immediate clamping of the umbilical arteries, followed by gentle stripping of the umbilical vein. This procedure disrupts the blood supply to the placenta and results in an exsanguination into the body of the infant, there occurring a conservation of blood which otherwise would remain in the placenta or be spilled, if one practices the method of bleeding the placenta in order to facilitate its separation and expulsion.

I have frequently observed that in cases of asphyxia administration of oxygen to the mother improves the color of the infant. For this reason I have not clamped the umbilical arteries until the newborn infant cries. However, my observation may be erroneous, as excellent recent work seems to prove the immediate separation of the placenta in all normal cases, with rare exceptions. This being true, such an early disconnection with the maternal oxygen source would make unnecessary any hesitation in clamping of the arteries.

Observation has convinced me of the rapid depletion of blood in the umbilical vein and placenta. On many occasions I have compressed the placenta, after its delivery, and milked its surface veins with noticeable increased diminution in the amount of contained blood. I believe I have seen the infants' color improve.

In most cases the umbilical arteries are easy to define and clamp. In large cords a single blade of the hemostat is made to pierce the cord adjacent to the vein, and all tissues except the vein are clamped.

My observations have been such as to make insecure any conclusions I have drawn. This small contribution is offered in the hope that it might interest someone whose volume of work and access to proper facilities for measurements justifies a conclusion on this method of handling the cord.

G. M. A. FORTIER, M.D.

REFERENCES

1. Titus, Paul: *The Management of Obstetric Difficulties*, St. Louis, 1940, The C. V. Mosby Co., ed. 2, p. 850.
2. Serbin, W. B.: *S. Clin. North America* 23: 73-83, 1943.
3. O'Conner, Cornelius T.: *AM. J. OBST. & GYNEC.* 48: 683, 1944.

LITTLE FALLS, MINN.

DEC. 18, 1944.

Items

Melbourne W. Boynton, M.D., A War Casualty

Colonel Boynton, of Chicago, instructor in obstetrics and gynecology at the Lying-In Hospital, a diplomat of the American Board of Obstetrics and Gynecology, was killed Aug. 19, 1944, as the result of an experimental parachute jump which was to record the effects of a free fall of 35,000 feet. Interested in aviation, he was rapidly advanced in rank and became head of the medical division of the Office of Flying Safety in the Army Air Services. Dr. Boynton was a member of the Chicago Gynecological Society.

American Board of Obstetrics and Gynecology

Examinations

All candidates will be required to take both the Part I examination and the Part II examination (oral-clinical and pathology examination). Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held later in the year.

Notice of the exact time of the Part II examination will be sent all candidates well in advance of the examination date. Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

If a candidate in Service finds it impossible to proceed with the examinations of the Board, deferment without time penalty will be granted under a waiver of our published regulations as they apply to civilian candidates.

Applications for the 1945 examinations are now closed.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

Necrology

FRANK WORTHINGTON LYNCH, M.D., obstetrician and gynecologist of San Francisco, Calif., died Jan. 12, 1945, of a heart attack at the age of 73 years. Dr. Lynch was born in Cleveland, Ohio, 1871, a graduate of Johns Hopkins, 1899, where he then served as resident, instructor, and associated obstetrician before settling in California. He became Professor of Obstetrics and Gynecology at the California University and after his retirement was made an Emeritus. He was a Diplomat of the American Board, a former President of the American Gynecological Society and the Pacific Coast Society of Obstetricians and Gynecologists, and member of several leading specialist societies as well as a Governor of the American College of Surgeons. Dr. Lynch was the author and co-author of various medical works, a frequent contributor to the literature, and a member of the Advisory Editorial Board of the JOURNAL since its inception.

WALTER PONDER CONAWAY, A.B., M.D., Senior Attending Gynecologist at the Atlantic City Hospital, died at his home after a long illness Jan. 12, 1945. Born in Leipzig, Del., in 1871, graduated in Medicine at the University of Pennsylvania, a member of many professional societies, he was president of the Medical Society of the State of New Jersey in 1927, a Fellow of the American College of Surgeons, and a Diplomat of the American Board.

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CARCINOMA OF THE CERVIX AND PREGNANCY*

A Clinical Study of Eight Cases

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CARCINOMA of the cervix occurring during pregnancy is a tragic complication. In the past five years, we have observed eight such cases on the obstetric services of Cook County Hospital. These patients were distributed as follows: The first one was seen in 1939, the second in 1941, and the last six in 1943. This unusual increase in the last year has impressed the entire personnel of our department that this is a complication for which we must always be on the alert.

Etiology and Pathogenesis

During pregnancy, one rarely observes carcinoma of the cervix. Carcinoma appears in appreciable numbers in an age group when the child-birth incidence has decreased decidedly. In our series of patients, the youngest was 25 and the oldest 43 years of age. All except the youngest were older than the average age of the rest of our obstetric patients.

Due to the uneven distribution of our series, whereby three-quarters of our cases appeared in one year, we did not attempt to establish a percentage incidence at Cook County Hospital. Danforth,¹ in an analysis of accumulated figures, finds the frequency to be about 0.032 per cent. Baer² states that one in 10,000 pregnancies represents the general average with an explanation for its infrequency to be found in the alterations in the cervix by the carcinoma so that "Fertilization may thus be prevented mechanically, chemically or because coitus becomes impossible or repulsive."

*Presented at a meeting of the Chicago Gynecological Society, February 18, 1944.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

It is well known that most of the patients exhibiting carcinoma of the cervix are multipara. Parturition and abortions are the most frequent causes of lacerations, infection and erosion of the cervix. These changes are believed by many to make a favorable background for the development of cancer of the cervix at a later date. In this series, the ratio of multipara to primipara was three to one, whereas in all the rest of our pregnant patients, it is only about five to three. In a study of many other reports, we noted that the occurrence of cervical carcinoma was even much less frequent in women having their first pregnancy. Hofbauer,³ in a histologic study of apparently normal cervixes during pregnancy, found epithelial proliferation which was similar to premalignant phenomena seen in other organs, and which is regarded by him to be a factor in the possible production of malignancy at a later date. Perhaps a deflection of these proliferative changes in the cervical epithelium may be a precipitating factor of malignant development during pregnancy, since the whole endocrine mechanism is then profoundly altered.

While no race is immune to carcinoma of the cervix, an interesting observation in our small series indicated that this malignant growth might be more prone to occur during pregnancy in the white race. White patients outnumbered Negroes by 5 to 3, whereas in the same period of time, a tabulation of all the rest of our patients indicated that Negroes were in excess in proportions of about 2 to 1.

Pathology

The altered physiology of the cervix during a pregnancy must considerably influence a malignancy originating therein. It is believed by many that the carcinoma precedes the pregnancy, and is only a small growth at the time of conception. The malignancy is usually a squamous cell growth, but may in about ten per cent of cases originate from the glandular portion of the cervix.

The histologic pathology of the tumors, in all cases except one, was studied from the biopsy. While small tissue specimens serve their purpose well in establishing the diagnosis, one may be frequently led astray in using them for speculating upon the malignancy potential. For this reason, we made no attempt to grade the tumors pathologically.

Our material was studied with hematoxylin and eosin stains, and most of them had evidences that the tumor tissue grows in a very vascular field as indicated by numerous dilated blood vessels (Fig. 1). The connective tissue stroma is small in amount, and numerous mitotic figures are seen. In some specimens many polymorphonuclear and lymphocytic cells were seen around the clusters of malignant cells. One of our biopsy specimens showed that the neoplasm was extending into the adjacent anterior vaginal squamous cell epithelium (Fig. 2). An adenocarcinoma was noted only once in our series. This was the patient that lived only three hours after admission and at autopsy the chief findings were an ulcerated intrinsic carcinoma of the cervix infiltrating the surrounding pelvis and urinary bladder, and with small metastases to the periaortic lymph nodes. The mucosa was entirely missing and replaced by a necrotic granular membrane. Beneath the membrane and extending throughout the entire wall were numerous dark-staining irregular glands. Between the latter there was more connective tissue than noted in our other cases. In places, the dark-staining cells lost their glandular arrangement and were replaced by solid cords. When the patients carried their pregnancies into the last trimester the neoplasms attained

large proportions, and most frequently (5 out of 7) were of the evertans type of growth as a vascular cauliflower-like tumor. A study of our tissue specimens as a group gave us the impression that there was a definite trend to anaplasia with a loss of polarity of the cells rather than a maturity in the histologic pathology (Fig. 3).

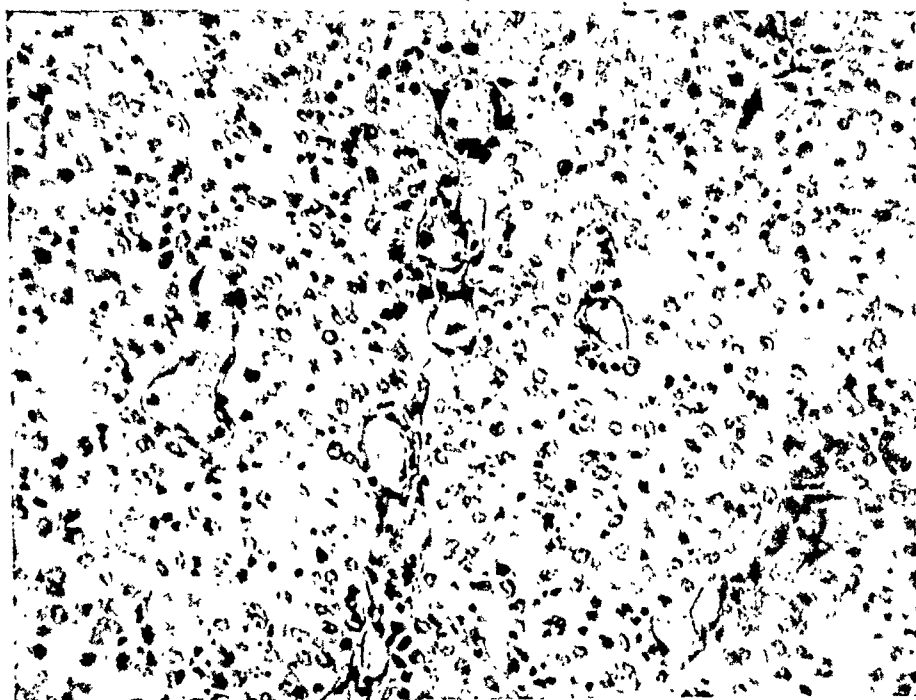


Fig. 1.—Numerous dilated blood vessels demonstrating the vascularity of the carcinoma (Case 5). $\times 126$.

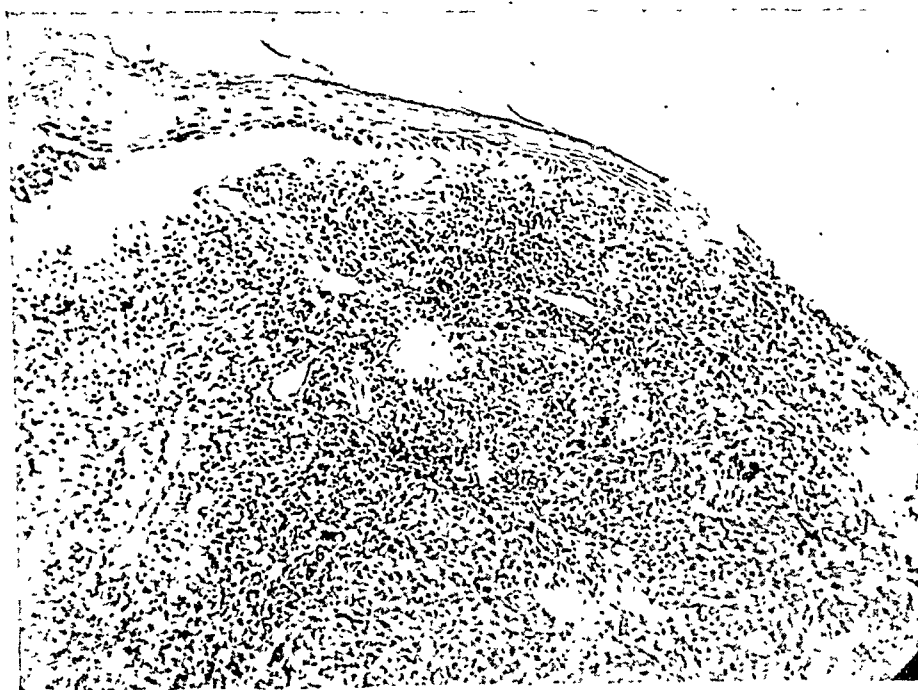


Fig. 2.—Carcinoma cells growing close to the vaginal mucosa anterior to the cervix (Case 1). $\times 33$.

Case Histories

The clinical features of cancer of the cervix during pregnancy, as noted in our series, may be brought out in a brief résumé of their case histories. They are presented in accordance to the period of gestation that the diagnosis was established, because the problem and its management thus differs.

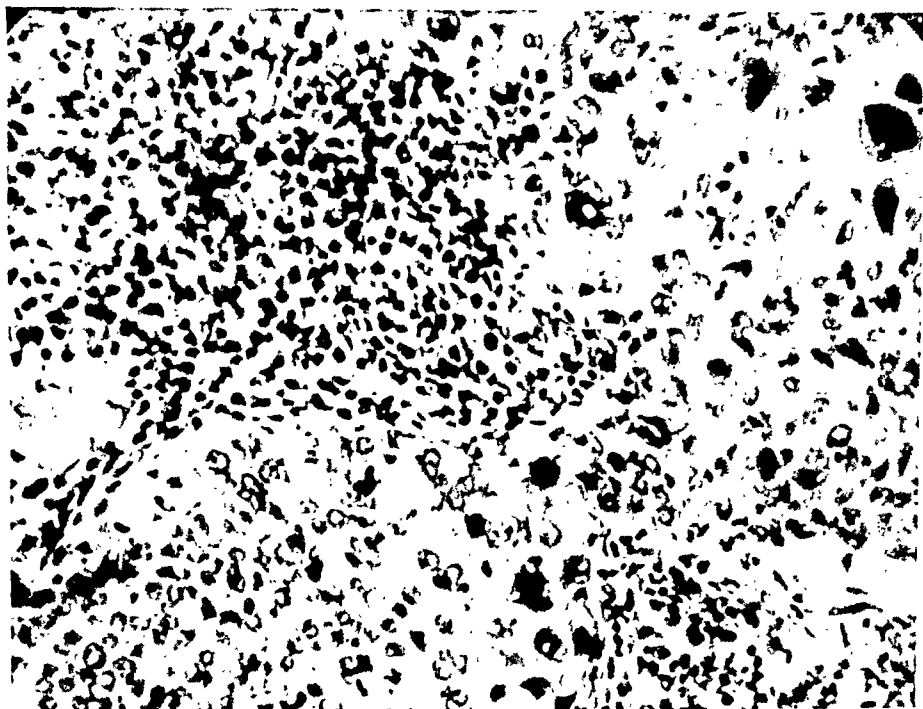


Fig. 3.—Anaplastic character of the carcinoma (Case 4). The cells are seen varying in size and shape, there is also a hyperchromasia, mitotic figure (below center) and a giant cell (upper right corner). $\times 300$.

Carcinoma During Early Pregnancy

CASE 1.—C. H., white, 35 years of age, gravida vi, para v, began prenatal care when she was about ten weeks pregnant. Her last menstrual period was 7/17/43, and in her second month, she bled a moderate amount which lasted for about one hour. This was a spontaneous bleeding with no relationship to any preceding event. A routine vaginal examination revealed that there was a hard nodular growth on the anterior lip of the cervix about 1.5 by 2 centimeters. This growth was closer to the anterior vaginal wall, and where the latter joined the cervix, there was a narrow, transversely directed superficial ulceration that bled moderately following the examination. There were no parametrial changes. A biopsy from the nodular portion of the cervix and the adjacent reflecting anterior vaginal mucosa revealed an infiltrating nonhornifying squamous cell carcinoma involving the cervix and the adjacent vaginal wall. She was referred to the department of radiotherapy, where in four weeks, she received 19 deep x-ray treatments for a total dosage of 2,850 r.* to the cervix through 4 external fields. The uterus then appeared smaller, the Friedman test was negative, and the patient was sent in for radium therapy. On 12/8/43, 1,500 mg. hours of radium were given. The next day, she developed abdominal pains and

*The r. dosage referred to above, or hereafter, will indicate the number of r. units delivered to the cervix itself as computed by depth dose charts.

24 hours thereafter, she extruded a macerated fetus which was evidently dead for a long time. The placenta delivered 24 hours after the extrusion of the fetus. Examination now showed that the nodule in the anterior cervical lip had definitely decreased in size, the small area of ulceration anterior to it had healed, and the parametria were not indurated. Four weeks later, she received two more radium treatments to make a total of 4,500 mg. hours. She is still under observation receiving deep x-ray therapy. Barring unforeseen complications, her prognosis at this time appears to be favorable.

Carcinoma During Late Pregnancy

CASE 2.—L. G., Negro, aged 33 years, gravida i, last menstruated 8/6/38. Prenatal care began in her third month and routine vaginal examination failed to reveal anything significant. Wassermann test was positive and she received antiluetic treatment. She had a moderate blood pressure elevation on 2/21/39, and was admitted on 4/11/39 with complaints of headaches, a trace of albumin, and a blood pressure elevation which ranged from 140 to 160 systolic, and a diastolic level of 90 to 110 mm. Hg. The patient had no edema, and her fetus appeared smaller in size than the period of gestation would indicate. Four days later, the fetal heart tones could not be heard. A medical induction was tried and twice failed. A bag induction because of persistent blood pressure elevation and a retinal hemorrhage was attempted (4/17/39). The cervix was felt to be definitely abnormal. The anterior lip was soft, irregularly polypoid and friable. The posterior lip, which was indurated, felt like a band that was parallel with the external os. Pieces of the friable tissue broke off and were sent to the laboratory for examination. The bag of waters ruptured during this examination, and a pulseless cord that prolapsed was cut off. The pathology report of the tissue was "nonhornifying squamous cell carcinoma of the cervix." The patient's temperature rose to 102.4° F., and the pulse 140 per minute. The discharged amniotic fluid became purulent and had a very offensive odor. On 4/20/39, the fetus and uterus were removed together as one would remove a huge fibroid. The supracervical portion of the uterus was amputated between clamps to avoid spill of infectious substance. The patient had a stormy postoperative course. The incision became superficially infected and broke down. A puerperal pyelitis developed on the tenth day postoperative. In six weeks she was getting deep x-ray therapy followed by two treatments of radium totaling 3,000 mg. hours. In a period of 17 months, she received 69 roentgen treatments for a total dosage of 17,275 r. of which 9,100 r. was through an intravaginal cone and 8,175 r. through 6 external portals. When seen one year later, she had no trace of the original tumor. Two years later, she had a bowel obstruction that cleared up without any operation. She never returned thereafter. We were informed that she left Chicago three years after the operation in poor health to return to her home in the South. It is our opinion that she had a recurrence, and probably died shortly after leaving the city.

CASE 3.—L. W., Negro, aged 31, para iv, gravida vii, last menstruated 5/20/40. Prenatal care began in the third month, but no significant findings were noted concerning the cervix. She spotted blood frequently during pregnancy and in her sixth month (11/26/40) she was admitted to the hospital for a suspected placenta previa. The obstetrical resident recorded that the cervix was large and purplish in color, and

that "a large erosion on the anterior lip" bled rather profusely on contact. This was readily controlled by a silver nitrate stick application, and she was discharged two days later. She was again admitted on 1/18/41, as a multipara in labor. She bled rather profusely shortly after this admission, and vaginal examination revealed a large, fungating, punched out, red, raw area, 3 by 4 cm., on a very large hypertrophied anterior cervical lip. This was dark blue and was so indurated, that it had a cartilaginous feel. The parametria were not infiltrated. A biopsy of this suspicious area revealed "an infiltrating nonhornifying squamous cell carcinoma." On 1/24/41, a Porro cesarean section and bilateral salpingo-oophorectomy were performed. Postoperative recovery was good and the patient was discharged on the thirteenth day, with instructions to return to the Gynecology Tumor Clinic, where patients for pelvic radium therapy are managed. This patient did not go to the tumor clinic as instructed, but went to the Outpatient Radiotherapy Clinic, where in a period of four and one-half months she received 65 x-ray treatments through six fields for a 10,000 r. dosage, but never any radium treatment. Despite regular x-ray treatments, which began shortly after her discharge from the obstetrical department, she had a progressively downhill course. On 9/24/41, she reappeared in the gynecology department because of considerable vaginal and rectal bleeding. A tumor mass filled the entire pelvis. She was given palliative treatment, but continued to bleed intermittently. She died ten months after her delivery, but no postmortem examination was permitted.

CASE 4.—B. F., Negro, aged 32, para i, gravida ii, last menstruated on 5/25/42. Her first prenatal examination was in her sixth to seventh month at another clinic, where a certified obstetrician who examined her noted that the cervix was badly eroded and lacerated, and bled freely. Nevertheless, he failed to regard this as significant and on 2/28/43, she passed several blood clots and noted that when she urinated, she would bleed profusely. One hour later, she was admitted to the obstetric service and a tentative diagnosis of placenta previa was considered. Vaginal examination revealed a posterior cervical lip replaced by a large cauliflower-like mass about 7 by 4 centimeters. The mass had a broad base, was irregular and the surface bled on the least contact by gauze or cotton. The left parametrial zone definitely felt infiltrated. A biopsy revealed an anaplastic nonhornifying squamous cell carcinoma of the cervix. The tumor mass bled off and on. A classical cesarean section was performed on 3/2/43, at 7:00 P.M. Her temperature was 100.4° F., and pulse 96 per minute in the afternoon. From the operative field, the mass could be seen extending up the cervix. It was bleeding and was only controlled by a pressure pack that was inserted vaginally. For the next three days, the temperature ranged up to 101° F. The abdomen was markedly distended and the pulse spiked to 120 and 140. The highest temperature elevation was 102.2° F. on the sixth day, and gradually declined. During this period, she had received two blood transfusions and sulfathiazole. On the eighth day, a catheterized specimen of urine showed pus cells in clumps, but after the tenth day, the temperature remained normal. On 3/26/43, she was discharged and referred to the tumor clinic. The baby had died within 24 hours from an aspiration pneumonia. X-ray treatments for the mother were started three days before discharge. She had only 14 radiation treatments, and she did not attend the tumor clinic as advised, and never returned in spite of all efforts to contact her.

CASE 5.—B. B., white, aged 38, gravida xv, para x, last menstruated 6/24/42. She had no prenatal care and was admitted to the hospital when she was about five and one-half months pregnant for a possible threatened abortion. The bleeding promptly stopped with bed rest and she left the hospital six days later, but never reported to the prenatal clinic as instructed. She continued to bleed off and on which would necessitate bed for relief. On 2/28/43, she passed large blood clots and four days later presented herself at the hospital for readmission. She was now eight and one-half months pregnant. Upon vaginal examination, with precautions observed when a placenta previa is suspected, we found a markedly lacerated cervix and the anterior lip was chiefly involved in a markedly but irregularly hypertrophied, almost cauliflower-appearing tumor mass. It was very vascular, bled freely on touch, and had a firm cartilaginous feel. The entire cervix was almost four times the normal size. Some of the epithelium of the anterior lip was grayish in appearance resembling a surface necrosis. Biopsy of this mass revealed a nonhornifying squamous cell carcinoma. A classical cesarean section was performed on the second day in the hospital. The postoperative course was entirely uneventful. On the thirtieth postoperative day, the red count was 2.45 and the hemoglobin was 44 per cent. The only temperature elevation was 100° F. on the fourth day postoperative. She was given a transfusion of 500 c.c. of blood on the fifth postoperative day. X-ray therapy was started the sixth postoperative day, and she was discharged from the hospital on the sixteenth day with instructions to return for a continuation of radiation therapy. She was readmitted in two months after her discharge to the gynecology ward, and the tumor mass, despite thirty-four treatments of radiation, had become very far advanced, and the pelvis was "frozen" so no radium therapy was used. The patient continued to receive deep x-ray therapy for a total of 60 treatments through 6 external portals for a total dosage of 9,000 r. She was last seen again in the gynecology ward on 12/1/43, in a terminal condition.

CASE 6.—A. V., white, gravida iv, para iii, was under the care of a private doctor. She was admitted to the obstetric ward on 7/29/43, when she was apparently almost full term. She had no pains, but came to the hospital because she had slight bleeding at 7:30 that morning. Her membranes ruptured at 10:30 A.M. and mild pains were noted. The bleeding was interpreted by the resident staff to be a possible bloody show. A vaginal examination revealed a cauliflower mass that was hard, friable and bled with the least manipulation. A biopsy revealed a nonhornifying squamous cell carcinoma. On the evening of admission, a classical cesarean section was performed under local anesthesia. The postoperative course was entirely uneventful. The highest temperature was 100.2° F. on the seventh day. X-ray therapy was started on the sixth day, and she received 3 irradiations when discharged on the fifteenth postoperative day. She was given 60 radiation treatments between 8/4/43, and 11/27/43, through 6 fields for a total dosage of 7,000 r. The tumor clinic following the course of this patient examined her eight weeks after her operation, and found the entire posterior cervical lip was replaced by a craterlike ulcer which was continuous with an induration posteriorly in the direction of the rectovaginal septum. The parametria were fixed. With these findings, radium treatment was deemed to be unwise since a rectovaginal fistula was very likely to occur. The only treatment available would be palliation by further use of deep x-ray therapy.

CASE 7.—M. S., white, gravida vi, para vii, aged 43, had no prenatal care. She was admitted to the obstetric service on 9/3/43, with a history of bleeding for the past four weeks. During the week prior to her admission, the bleeding had become very marked, and she did not feel life after that time. On the day of admission, she had cramplike pains that were not typical of labor pains. Her condition was very poor. She was in profound shock; her blood pressure was 50 systolic and 35 diastolic. Although she received 500 c.c. of plasma, 1,000 c.c. of blood and 1,000 c.c. of saline, she did not rally. A vaginal examination revealed that the entire cervix was very hard and markedly eroded, and was covered by a shaggy, gray, friable tissue over the whole of its canal. The structures adjacent to the cervix were infiltrated with especial involvement of the posterior wall of the bladder. The patient expired three hours after admission. At autopsy, the essential anatomic findings were: 1. Ulcerated intrinsic carcinoma of the cervix with infiltration into the surrounding pelvis and urinary bladder. 2. Intact seven-month pregnancy with a macerated fetus presenting a breech at the inlet. 3. Small metastasis to the left periaortic lymph nodes. The histopathologic findings of cervix revealed an adenocarcinoma with areas where the cells lost their glandular arrangement and formed solid cords.

Carcinoma of the Cervix First Noted in the Puerperium

CASE 8.—A. R., white, 25 years of age, gravida i, who had no prenatal care, last menstruated on 11/14/42. She was first seen when she was in labor at full term on 8/3/43. A normal baby, weighing 6 pounds, 14 ounces, was born after seven hours and twenty-five minutes of labor. There was no postpartum hemorrhage and puerperium was uneventful. She was out of bed on the sixth day and was discharged the next day. She returned for a routine postnatal examination after eight weeks of puerperium, during which time she had no significant symptoms. A vaginal examination revealed that the entire posterior cervical lip had been replaced by a fungating polypoid mass which was in contact with the posterior fornix, but was not adherent to it. The parametrium was soft without the slightest bit of induration. The corpus was normal in size, shape, position and mobility and there were no palpable masses in the adnexal zones. A biopsy from this mass was misplaced and the patient had six deep x-ray treatments before another was obtained. The histopathologic picture was essentially that of a squamous cell carcinoma of the cervix, which had rudimentary hornification and some giant cells. After 28 treatments for a total of 4,200 r. through six fields, she was admitted to the hospital. At this time, which was almost two months after the first puerperal examination, the only additional finding was a slight fixation of the left parametrium. She received a total of 4,500 mg. hours of radium in three divided doses, and was referred back to the x-ray department for more deep radiation therapy.

The Clinical Picture

Carcinoma of the cervix is usually small in size at the time of conception. Unfortunately, it may be a silent clinical entity for a long period of time. In the nonpregnant state, one may in a routine or periodic examination occasionally discover the malignancy at a very early stage. During pregnancy, the prospect of an early diagnosis is less likely due to aversion on the part of obstetricians to re-examine

pregnant patients vaginally. Another factor interfering in the diagnosis is a fixed assurance that cervical carcinoma is unlikely to occur. Thus, the growth may virtually become enormous in the last trimester or in puerperium. This was our experience as exemplified in the tabulated clinical data. The only significant symptom attributable to the cancer during pregnancy is *painless bleeding* that occurs in varying amounts. This symptom was only absent in two of our patients, but in six it was found to have been present in variable amounts and with a tendency to recur. It was noted in one patient as a *scanty bleeding* in the first trimester; in four women in the second trimester, but the real cause remained unsuspected; in one, the bleeding did not develop until she was close to full term; and in one patient, who was admitted exsanguinated and died shortly after her admission. Obviously, carcinoma is too often far from a consideration as a cause of bleeding during pregnancy. In our series, the cause of the bleeding was attributed to erosion two times, and once to threatened abortion. When the true cause of their bleeding was finally determined, their pregnancies had advanced to the last trimester of gestation and the tumor had become very large. Their admittance diagnosis to the hospital at this time was placenta previa.

The cervical changes in all our patients were significant. The degree of cervical involvement noted depended on the period of gestation that the carcinoma was diagnosed. The anterior cervical lip of a patient 10 weeks pregnant was moderately enlarged, and felt very hard. On speculum examination, a small amount of bleeding was seen to arise from a superficial ulceration where the anterior vaginal wall joined the cervix. This tumor diagnosed was the smallest of any in our series. In two cases that were seen in the second trimester of pregnancy but not diagnosed, the cervix was definitely enlarged and appeared beefy and eroded. For those patients who were not diagnosed until the last trimester of pregnancy, the cervical findings usually consisted of a large cauliflower-like mass that had replaced a great part of the cervix, and bled readily on any manipulation. The carcinoma tends to decrease in size in the first three weeks after abdominal delivery. This was noted in two patients, and it is perhaps due to a disappearance of some of the edema and congestion that are present in the cervix prior to childbirth. In five patients (including the one diagnosed in early pregnancy), the parametria were free from induration and grossly would fit into Group 2 (Schmitz). One patient had some parametrial involvement and she would be placed in Group 3, and the patient who was admitted moribund was in Group 5. These growths bled very readily on manipulation, but the discharge was not offensive and necrosis of the neoplasm was not very evident, probably due to the more abundant blood supply during pregnancy.

Thus, from our experience, the two consistent symptoms were painless bleeding and the local vaginal findings. During early pregnancy,

TABLE I. COMPARATIVE CLINICAL DATA

CASE	AGE	PARITY	RACE	PRENATAL CARE	SYMPTOMS DURING PREGNANCY	ADMITTANCE DIAGNOSIS	GESTA-TION WHEN CA. WAS DIAG.	CERVICAL FINDINGS AND PATHOLOGY	DELIVERY	TREATMENT; SUBSEQUENT COURSE
1 (C. H.)	35	Multip. (5)	White	Began 2½ months	Slight bleeding before and at 1st visit.	For biopsy of cervix.	10 to 12 weeks	Small nodular growth on ant. cerv. lip near vagin. reflection. Nonhornifying squamous cell carcinoma.	Aborted following radium treatment.	19 x-ray—2,850 r. first 4 weeks. 4,500 mg. hr. radium (3 divided doses); is still receiving radia-tions. Prognosis is favorable.
2 (L. G.)	33	Primip.	Negro	Began 4th mo. Wassermann positive antiluetic treatment	Hypertension (no bleeding).	Hypertension (nephritis).	7 to 8 months	Moderate sized growth; anterior lip friable, posterior lip indurated. Nonhornifying squamous cell carcinoma.	Fetus dead. B.O.W. rupt. Intrauterine infection. Supravaginal hysterectomy fetus in uterus.	Stormy P.O. course. 69 x-ray treatments 17,275 r. 3,000 mg. hr. radium. Probably died 3½ years later.
3 (L. W.)	31	Multip. (4)	Negro	Began 3 to 4 mo. (outside clinic)	Bleeding erosion in 6th month (was admitted to hosp.)	Labor pains profuse. Bleeding after admission. Placenta previa.	8 months	Large fungating raw area on ant. lip. Infiltrating nonhornifying squamous cell carcinoma.	Porro cesarean.	Uneventful P.O. course. 65 x-ray treatments—10,000 r. Profuse vaginal bleeding 8 mo. later. Died 10 mo. P.O.
4 (B. F.)	32	Multip. (2)	Negro	Began 6 to 7 mo. (outside clinic)	Bleeding erosion at 1st visit.	Bleeding. Placenta previa.	Almost full term	Large cauliflower-like mass in post. lip, infiltrated left parametrial zone. Anaplastic nonhornifying squamous cell carcinoma.	Classical cesarean section. Cervical bleeding persisted at operation.	Cervix packed to stop bleeding. P.O. course rather stormy. Highest P.O. temp. 102.2°; pyelitis on 10th P.O. day. Baby died on 2nd day. Patient uncooperative, and did not return for subsequent treatment as directed.

5 (B. B.)	38	Multip. (10)	White	None	Bleeding— admitted in 5 to 6 mo. as threat- ened abor- tion. Bled intermit- tently.	Bleeding. Placenta pre- via.	Almost full term	Large cauliflower-like mass. Nonhornifying squamous cell car- cinoma.	Classical cesar- ean section.	Uneventful P. O. re- covery. Tumor mass not affected by radi- ation. Frozen pelvis in 2 mo. 60 x-ray treatments 9,000 r. In terminal condi- tion 9 mo. after de- livery.
6 (A. V.)	38	Multip. (3)	White	Private doctor	None record- ed.	Bleeding prior to ad- mission.	Almost full term	Large cauliflower-like mass. Nonhornifying squamous cell car- cinoma.	Classical cesar- ean section.	Uneventful P. O. re- covery. 2 mo. later infiltration of recto- vaginal septum. 60 x-ray treatments 7,000 r. Prognosis poor.
7 (M. S.)	43	Multip. (6)	White	None	Bleeding se- vere 4 weeks before ad- mission.	Exsanguin- ated, pro- found shock.	7 months	Large ulcerated mass, infiltrating bladder. Adenocarcinoma of cervix.		Died undelivered. Massive carcinoma with extension to bladder and metas- tasis to pelvic lymph nodes.
8 (A. R.)	25	Primip.	White	None	None.	Normal labor.	Full term	At postnatal exam. 8 wk. P.P. posterior lip has large cauli- flowerlike mass. Nonhornifying squamous cell car- cinoma.	Spontaneous delivery.	Still under treatment. Has received 4,500 mg. hr. radium and is getting deep x-ray treatments. Second month after onset of therapy, left par- ametrium slightly infiltrated.

the bleeding must be differentiated from a threatened abortion, or a bleeding nonmalignant erosion. The bimanual palpation of a hard mass that is irregular and bleeds readily should always be followed by a biopsy that might determine the diagnosis. *Any pregnant patient with persistent cervical bleeding should have the same diagnostic biopsy that the nonpregnant patient is accorded.*

Prognosis

There is a strange divergence of opinion in the medical literature concerning the influence that pregnancy exerts on the growth of cancer of the cervix. Some observers claimed that gestation inhibited the growth of carcinoma of the cervix or at least did not act unfavorably, and based their belief on the ease of operability and the early stage that the neoplasm might be found during a pregnancy (Mankin,⁴ Smith,⁵ Stöckl,⁶ Weibel⁷). On the other hand, some observers contend that local genital hyperemia, increased glycogen content of the genital tissues, and the earlier age of the patient might cause the carcinoma to grow faster. We agree with Danforth,¹ Baer,² Brouha and Gosselin,⁸ and Nevinny⁹ that the malignancy is not inhibited during pregnancy but possibly accelerated in its rate of growth. Hemorrhage during pregnancy or parturition is a hazard to the patient. If the patient survives the hemorrhage or sepsis, there is the ever gloomy prognosis concerning the growth of the tumor after childbirth. Childbirth trauma is certain to cause the carcinoma to flourish at a greater rate. McNeil¹⁰ has observed that the earlier age group, such as these patients are in, is associated with a greater degree of malignancy of the new growth.

When the diagnosis is made early in pregnancy and is immediately followed by vigorous treatment, a much better prognosis may be expected. Thus, Peham and Amreich,¹¹ and the tabulated cases in the recent report of Maino and Mussey¹² indicated that a great majority of 5-year or longer cures were found in those patients in whom the diagnosis was established early in pregnancy. In our own limited series, it is obvious to us at least, that patients diagnosed for the first time in late pregnancy had large tumors and despite vigorous therapy that was immediately instituted, their prognosis is poor.

Another factor militating against the ultimate outcome of these unfortunate patients is the delicacy with which the patient is apprised that her condition is serious. In a large clinic, where the social and intelligent strata of the patient are lower, she must at times be informed more directly as to her true condition. Where the patient's feelings are held with delicacy, the patients, such as seen in our clinic, soon lose interest in the inconvenience that the follow-up treatment entails. Our patients move frequently and are soon lost. We feel that the lack of the necessary intensive treatment in three of our patients may thus be explained.

Treatment

During the past two decades, the swing from radical surgical removal to conservative radiation therapy has received wide recognition. During pregnancy, the treatment is only altered by the problem of the disposition of the fetus. It is felt by many observers that the trauma ordinarily sustained by the cervix, by the mechanics of parturition, may seriously affect the cervix that contains a cancer. Therefore, with the amount of injury being unpredictable where the extent and exact degree of involvement of the tumor is unknown, we prefer to spare the cervix of the trauma of labor. The one patient who had no symptoms during pregnancy, and had an easy labor with no hemorrhage or any sepsis, nevertheless, on her first postnatal visit had a large growth that was in Group 2, and two months later, despite radiation, had become a Group 3 (Schmitz classification).

Those who favor cesarean section in the last trimester of pregnancy may not agree as to the disposition of the fundus. Danforth and Baer would prefer a routine Porro cesarean section because of potential sepsis, and Danforth adds that the possibility of pyometra is obviated. In performing a cesarean section, with or without a hysterectomy, the carcinoma still remains with the patient. Since her ultimate recovery hinges on the therapeutic effect of radium and deep x-ray on the carcinoma in the cervix, profound thought must be given to whether routine removal of the fundus is best for the patient.

The selected manner of abdominal delivery should be one that will facilitate the radium therapy that is given at a subsequent time. A Porro cesarean leaves a cervical stump that is not as effectively treated by radium as a cervix that has a corpus to retain a capsule of radium for crossfire effect. Then again, the bladder assumes a different relationship and may, in being brought over the cervical stump, be involved by radium ray emanation despite its limited field of penetration. Another objection to a supracervical hysterectomy lies in the unpredictability of the histologic extent of the carcinoma. One may cut through malignant cells, or place sutures therein when the cervical stump is closed. It is for these reasons that we prefer an elective classical cesarean section and are in accord with Beck,¹³ Titus,¹⁴ McNeil¹⁵ and Schmitz.¹⁶

We advocate a Porro section when the patient is infected as indicated by the type of vaginal discharge, purulent or not, and the oral temperature of the patient. Thus, the indication for the Porro section is the presence of a known sepsis, not the presence of a carcinoma in itself. Three of our patients had a classical cesarean section. One of them had cervical bleeding that was only controlled by gauze sponge packs, inserted from below. A supracervical amputation of the uterus would not have affected the source of bleeding, and she was in no condition for a complete hysterectomy such as a radical Wertheim (see Case 4).

In general, the treatment we follow is the one Danforth and Baer have proposed, with exception that the uterus should not be removed in the last trimester of pregnancy, except where there is an active intrauterine infection present. Thus, in early gestation, we ignore the pregnancy. We advocate first deep x-ray treatments to irradiate a wide field within the pelvic sphere, and after the death of the fetus, radium to be inserted, giving a total of 4,500 mg. hours, and then to follow up the therapy with many more deep radiations.

When a patient is first diagnosed after the fetus is viable, we favor a classical cesarean section for reasons stated, and as soon as possible in the puerperium start deep radiations; and after involution of the uterus, radium to be given in 1,500 mg. hour doses, giving the patient three such treatments totaling 4,500 mg. hours. The deep radiation was 200 K.V. through six fields and a transvaginal approach whenever possible.

If the patient is reasonably close to having a viable baby, we agree with Baer, who advocates radium therapy first to retard the malignant growth and permit the fetus to attain a viable status before a cesarean section is contemplated.

General supportive treatment is an important phase of the therapy. The diet should be rich in antianemic factor. Where the blood picture indicates an anemia, transfusion is also very helpful. The patient should be impressed with the seriousness of her condition. A well-understanding social service in liaison between the medical division and the patient would be very helpful. The patient's relatives should be apprised of her real condition. The patient should be followed by the social service worker to see that she keeps up her schedule of treatment. Any failure on her part should make the medical or social service agent responsible for informing the patient more definitely concerning the true condition for which she is being treated.

Summary and Conclusions

Eight cases of carcinoma that appeared in the past five years during a pregnancy were clinically studied. The uneven distribution of these cases, whereby six were noted in one year would render untenable a statistical evaluation of its incidence on our services. Many white and Negro patients are seen annually in our hospital, and it appears that carcinoma of the cervix, at least during pregnancy, might be more frequent in white women. In seven patients the malignancy was a stratified squamous cell carcinoma and in one patient, who died undelivered, it was an adenocarcinoma.

There is a tendency to regard carcinoma of the cervix during pregnancy as so improbable that other causes of bleeding are given stubborn precedence in diagnosis and therapy. The malignancy is thus diagnosed more often toward the end of pregnancy, when the growth has achieved large proportions. Carcinoma of the cervix, contrary to the opinion

of several contributors, continues to develop at a rapid pace during pregnancy. The earlier the diagnosis is established the sooner effective therapy may be instituted, and the better the ultimate prognosis.

The treatment of these cases depends upon the disposition of the pregnancy. In the first trimester the pregnancy is disregarded and deep x-ray therapy is instituted. With the death of the fetus, radium is added to the treatment. In advanced pregnancy, there is added concern for the cervix. The latter should be spared of the injuries that occur during parturition. If there is no infection as noted by the temperature or character of the vaginal discharge, a classical cesarean section is performed to spare the cervix of trauma and to leave intact the fundal portion of the uterus to facilitate the radium therapy, which is started after uterine involution has occurred. A total of 4,500 mg. hours of radium is given in three equally divided doses. As soon after the delivery of the baby as possible, deep x-ray treatments are started, and continued for a long period of time. In the presence of local infection by criteria mentioned, a Porro cesarean section is preferred. In pregnancies close to viability the cesarean section may be deferred, and 1,500 to 3,000 mg. hours of radium may be given to the cervix to temporarily inhibit the progress of the new growth.

The ultimate prognosis for the patient hinges on the persistent continuation of the deep x-ray and radium therapy that is instituted after the disposition of the pregnancy. The patient must be apprised of the seriousness of her condition directly or indirectly. In a public institution, the follow-up is best attended to by a well-established social service department. When the patient fails to adhere fully to the program of the important follow-up therapy, it is the responsibility of the social service department, or the physician to inform the patient more directly of her exact condition.

We gratefully acknowledge the frequent advice and help by Dr. Herbert E. Schmitz of the Department of Gynecology.

References

1. Danforth, Wm. C.: *AM. J. OBST. & GYNEC.* 34: 365, 1937.
2. Baer, Jos. L.: *S. Clin. North America* 16: 51, 1936.
3. Hofbauer, J.: *AM. J. OBST. & GYNEC.* 25: 279, 1933.
4. Mankin, J. W.: *Arch. f. Klin. Chir.* 199: 337, 1940.
5. Smith, F. R.: *AM. J. OBST. & GYNEC.* 34: 616, 1937.
6. Stöckl, E.: *Ztschr. f. Geburtsh. u. Gynäk.* 101: 437, 1934.
7. Weibel, W.: *Arch. f. Gynäk.* 135: 1, 1929.
8. Brouha, M., and Gosselin, O.: *Gynécologie* 33: 776, 1934. (Quoted from DeLee and Greenhill: *Year Book of Obstetrics and Gynecology*, Chicago, 1935, Year Book Publishers, page 607.)
9. Nevinny, H.: *Ztschr. f. Geburtsh. u. Gynäk.* 99: 199, 1931.
10. McNeil, W., Jr.: *South. M. J.* 29: 940, 1936.
11. Peham, H. von, and Amreich, I.: *Operative Gynecology*, Philadelphia, 1934, J. B. Lippincott Company, Vol. 11, pp. 389-394.
12. Maino, Chas. R., and Mussey, Robt. D.: *AM. J. OBST. & GYNEC.* 47: 229, 1944.
13. Beck, Alfred C.: *Obstetrical Practice*, 3 ed., Baltimore, 1942, Williams and Wilkins Company, pp. 615-616.
14. Titus, Paul: *The Management of Obstetric Difficulties*, 2 ed., St. Louis, 1940, The C. V. Mosby Co., pp. 163-166.
15. McNeil, W., Jr.: *AM. J. OBST. & GYNEC.* 30: 414, 1935.
16. Schmitz, Herbert: Personal communication.

Discussion

DR. W. C. DANFORTH.—I agree that in most instances the carcinoma is present before the beginning of the pregnancy and do not believe that the essayists need be at any pains to explain the appearance of cancer in the two primiparous women. Carcinoma is not unknown in nulliparas and Miller has pointed out that the incidence in nulliparas does not vary as widely from that of multiparas as many of us have been accustomed to think.

I agree, on the whole, with the scheme of treatment suggested by the authors. In view of the fact that most advanced cancers of the cervix are infected, I should favor cesarean section followed by hysterectomy rather more often than do the essayists. When the cancer is not too extensive, the Ries-Wertheim extended operation may be considered, particularly in the earlier months of pregnancy. In the first trimester, unless the carcinoma is an advanced one, this may be regarded as an excellent form of management. Whether cesarean section only or section followed by excision of the uterus is chosen, the operation should be followed by efficient irradiation, both by means of x-ray and radium. In cases in which the carcinoma is found early in pregnancy, unless complete hysterectomy is chosen, the immediate employment of irradiation, without regard to the pregnancy, is the best treatment. In pregnancy sufficiently advanced that the fetus approaches viability, radium may be used for the purpose of retarding the progress of the cancer until the child becomes capable of extrauterine life. When this is done, as Murphy has pointed out, we must accept some risk of harm to the infant. In an occasional case in early pregnancy, in which the cancer is still in an early stage, total hysterectomy may be considered.

It is highly important that we recognize the danger of allowing delivery through a cervix in which the cancer has grown extensively. To allow the advanced presenting part to force its way through such a cervix exposes the woman to grave danger of hemorrhage because of laceration of the easily injured cervix, and to the certainty, if the patient does not die of hemorrhage, of extension of the cancer and of infection. Cervical incisions and manual dilatation cannot be considered.

Emge, in a paper published in 1934, expressed the opinion upon experimental and clinical evidence, that pregnancy exercises an inhibitory rather than a stimulating effect upon the growth of cancer. I, together with others, have felt that the contrary was probably true, but the number of cases seen by one clinician is too small to permit of a great degree of dogmatism. Stöckl believed that pregnancy neither accelerated nor delayed growth of cancer.

In some of the cases reported tonight, the presence of placenta previa was suspected because of severe bleeding. The likelihood of this confusion between the two has been remarked upon before. The presence of active bleeding calls for a determination of the cause. The essence of the management of carcinoma is early recognition. In view of this, and in the way of friendly and constructive criticism, may I allude to some of the facts of the case histories.

In Case 2, we find that the patient began prenatal care in the third month. At about the eighth month, she was admitted for toxemia. A bag induction was attempted, although it was found that the cervix was "definitely abnormal." At this time, a piece of friable tissue broke off. This was utilized for microscopic study. It is assumed that this procedure was in the hands of an intern or resident. The carcinoma was evidently an advanced one, but, had some one of greater experience recognized the cancer before the introduction of the bag, and had then proceeded to immediate removal of the uterus with the appropriate postoperative irradiation, would not the stormy convalescence have been less likely even though the ultimate result remained the same. The use of the bag is open to the same objections as those already stated when speaking of labor.

The third patient came under observation at the third month. She had frequent spotting and at the sixth month was admitted for suspected placenta previa. In other words, she was bleeding freely. The intern saw what he thought to be an erosion which bled profusely on contact. She was allowed to go home and was admitted at term in labor. At that time, a large carcinomatous mass was found in the anterior lip. The treatment from that point on may be approved. However, at the sixth month, had someone seen her whose gynecologic experience was sufficient to cause him to be aware of the fact that masses in the cervix which bleed easily may be malignant, treatment could have been initiated three months sooner. The marked contrast between the indurated carcinomatous area and the surrounding soft pregnant cervix has been mentioned by Tagliaferro, Sarwey and Bar, and this is in accord with my own experience.

In Case 4, the patient was not seen in the County Hospital until term but a "certified obstetrician" saw her at the sixth month and found an abnormal cervix which bled easily. I assume that "certified" means that he had passed the American Board. Perhaps, in his examination before that Board, the signs of cervical cancer were not discussed. The treatment given her after her admission to the hospital was entirely proper, but the doctor who saw her at the sixth month had an opportunity to do her a real service.

The patient in Case 5 entered the hospital at five months because of bleeding. After a few days' stay she went home, and again I assume that she was seen only by a resident or an intern. At eight and one-half months, she returned bleeding profusely. Again, treatment from this point on was efficient. Had the cancer been recognized at the earlier admission, the terminal condition in which she was when last seen might still have been her fate, but at least her chances would have been better.

It is probable that pregnancy begins in most cases when the cancer is relatively early. In late and far-advanced cancers, pregnancy is much less likely. Treatment is more effective the earlier it is begun. A review of the literature some years ago showed clearly that treatment is more effective in the first six months than in the last three. It is true that the rarity of the combination of pregnancy and cancer may cause the average practitioner to ignore the possibility of such a thing. The present report will help to bring the matter to our attention. It is to be regretted that the residents and interns were seemingly unaware that this combination may occur.

The report will cause all of us to increase our watchfulness. These cases, together with others reported at an earlier meeting of this Society at which this subject was considered, bring the number of cases reported in this city in the past few years to a number which must impress us with the fact that cancer in pregnancy is a complication which cannot be ignored.

In recognition and treatment in the earlier months of pregnancy lies the greatest, and almost the only, hope of cure.

DR. FREDERICK H. FALLS.—About six years ago, Dr. Danforth read a paper before this Society and Dr. Culbertson was asked to discuss it. He said that he could not discuss the paper because he had never seen a case. The President then asked for discussion from the floor, and there was but a handful of men in the room who had ever seen a case of carcinoma of the cervix in pregnancy. Now in a period of five years, according to this paper, eight cases of carcinoma of the cervix uteri and pregnancy have been observed in one institution.

My personal experience has been necessarily very limited. The first patient that I saw was at the University of Iowa. She came in for examination because of bleeding at about the eighth month of pregnancy and was dissatisfied because she was not examined immediately and left. She went to another clinic where placenta

previa was diagnosed, and a classical cesarean section was done. The carcinoma was not discovered while she was in the hospital, but only a few weeks after. She was then sent to our clinic where the diagnosis of carcinoma was confirmed, and she was given radium and x-ray treatment and died within a year.

Another patient with carcinoma came in after an abortion at five months. On examining her, we found a carcinoma which may or may not have been concerned with producing the abortion. This woman was given radium after thorough cauterization of the cervix. The carcinoma was about the size of a walnut. The radium treatment was followed by x-ray treatment. She was alive and in good condition two years after, and then was lost sight of.

The difficulty in managing these cases, it seems to me, hinges on the fact that nobody examined them during early pregnancy. No one recognized the carcinoma. Even with an evident ulcerating carcinoma, it was not recognized. Why should there be this vaginophobia? We do not advocate unnecessary vaginal examinations during pregnancy, but we know a speculum examination of the cervix can be done without danger and that it should constitute a part of every prenatal examination. Examinations should be repeated at any time during pregnancy that symptoms suggestive of carcinoma appear.

The question, of whether a Porro or a classical cesarean section should be done, is important. In one of these cases, several members of this Society were asked their opinion. My opinion was that a classical cesarean section should not be done, because as Whitridge Williams has pointed out, these carcinomas are always infected, and if a classical cesarean section were done, the streptococci and other organisms that were present would invariably produce serious sepsis. Dr. Kobak has now shown that those cases in which a classical section was done, did not develop sepsis. So while this is a very small series, it must be admitted that the *a priori* reasoning that cases will develop sepsis is not borne out by his cases.

There is a very poor prognosis in all of these cases that have progressed so far before treatment. Therefore, the only hope in such cases lies in seeing them very early in pregnancy and doing biopsies in any case in which the merest suspicion exists. Then, disregarding the pregnancy, one should do a total extirpation of the uterus.

The question of whether radium should be used when viability is approached should, I think, receive our attention. It seems to me that there is some danger of injuring the fetus or possibility of stimulating labor and producing abortion in a nonviable child. Since this is true, we feel that it is better to postpone any radiation treatment until the age of viability has been attained and then remove the fetus and the uterus.

This paper is a warning for those responsible for the training of men in both obstetrics and gynecology. If we have residents at the Cook County Hospital who get only obstetric training or residents in other clinics who see no gynecologic patients, we will always have men in charge of cases of this kind who are unable to make a diagnosis. Every obstetrician should be familiar with the course and clinical signs of carcinoma of the cervix.

In the event that the diagnosis is made early, does such a case belong on the obstetric or in the gynecologic ward? I think these cases should be primarily in the hands of gynecologists. As soon as the diagnosis is made, consultation should be asked and the obstetrician and gynecologist should decide what is best to do with that particular patient. If a total hysterectomy is indicated, she should be transferred to the gynecologic service. If a cesarean section is to be done, she should be retained in the obstetric service and be transferred a few days after delivery.

DR. RALPH A. REIS.—I would like to ask Dr. Kobak what the fetal salvage was in this series. He did not mention it in the paper.

I would like to emphasize what Dr. Falls said about so-called vaginal examination "phobia." In the last year, it has been my experience to see three patients taken to the operating room at the eighth month because of painless bleeding. One had a ruptured vulvar varix, a second had a polyp in the cervical sulcus and was not examined until very intensive bleeding appeared. I want to raise the question, whether it is not the feeling of most of us that a vaginal examination carefully done even in the face of threatening abortion can be kept a harmless procedure? I know two men in the group Dr. Danforth calls conservative, who will not examine a patient vaginally for fear the patient will miscarry. I do not think we can do intelligent obstetrics without a vaginal examination. If we cannot do that without causing abortion, then we do not belong in this specialty.

DR. J. E. FITZGERALD.—There seems to be some misapprehension as to the reason for presenting these statistics. I am sure you will agree that the principal reason for calling the attention of the profession to the occurrence of carcinoma of the cervix in pregnancy is that these cases are not diagnosed and for the reason Dr. Reis has given. If you will take Dr. Danforth's statistics on the incidence of carcinoma during pregnancy, there should be twenty cases in Chicago a year. If you accept Dr. Baer's idea (1:10,000) there should be six. Of the twenty cases that should have occurred last year, I am sure that most of them were not found. They were not found especially for the reason Dr. Reis gave.

There has been some criticism of the residents and interns. Having been told not to examine pregnant patients vaginally, the residents and interns do not do it. We have told residents and interns not to make vaginal examinations in a pregnant woman because an abortion or infection might result. We are perfectly convinced when we see a group as large as this in one year, that there are many carcinomas of the cervix that occur during pregnancy, and that the diagnosis is not made because of our fear either to do a vaginal examination, or to insert a speculum and find out why the patient is bleeding. Our reason for presenting these statistics is to see if more and more of the profession will not adequately examine pregnant women who are bleeding from the cervix, and thus give some help in the diagnosis of possible carcinomas.

DR. J. ROBERT WILLSON.—Since 1931, there have been six cases of carcinoma in pregnancy treated at the Chicago Lying-in Hospital. Four of these were diagnosed in late pregnancy and two in the puerperium. Only four occurred on our service, the remaining two being referred. During that time, there were approximately 45,000 deliveries, so the incidence of carcinoma of the cervix developing in pregnancy is 1 in 10,500 cases.

Four of the patients were treated more than five years ago, and are therefore eligible for the five-year survival statistics. Of this group, two or 50 per cent, survived at least five years. One had an early lesion and was treated by radium applications and deep x-ray therapy post partum. She is alive and well with no evidence of recurrence. The second patient who lived longer than five years was treated by predelivery radium and postdelivery x-ray therapy. She survived seven and one-half years, and died subsequently with an extensive malignant growth which was slowed down but not completely stopped by the treatment. Two of the patients lived less than five years. One refused treatment and survived twenty months. The other patient survived seven and one-half months after treatment was begun. The fifth patient was treated one year ago, and at this time, there is no evidence of extension of the initial lesion. The sixth patient is under treatment at present.

DR. KOBAK (closing).—The primary purpose of this paper was to show the pitfalls in diagnosis of a carcinoma during pregnancy. In the early months of gestation one finds the neoplasm is smaller, and therapy, radiation or surgical, is more likely to be successful. In the recent report of Maino and Mussey one finds support to this contention.

The superiority of radiation over surgery in treating carcinoma of the cervix has been shown in many clinics. The late Dr. Emil Ries, who was very skillful in the performance of the radical Wertheim operation, conceded before this Society that radium therapy was superior to radical surgery. We believe that this also holds for carcinomas that occur concomitant with pregnancy.

In our case reports errors that are very obvious in a posteriori reasoning are much in evidence. These mistakes were made by doctors not on the staff of Cook County Hospital as well as by our residents. The latter, as pointed out, did so by adhering to the popular phobia of vaginal examination, or regarded the malignancy as too improbable for a diagnosis.

Dr. Danforth referred to the patient who had a septic course. At no time did this patient present any symptoms or findings that could give a clue that a carcinoma was present in the cervix. Speculum visualization was apparently negative and there was no bleeding at any time. Her problem appeared to be the hypertension. When the fetal heart tones disappeared and several attempts at medical induction failed, we felt that the uterus must be emptied because of the persistently high blood pressure. Metreuryesis was contemplated, but when the resident found the cervix to be abnormal it was not carried out. True, the bag of water ruptured, a pulseless cord prolapsed, and sepsis followed, but all this was unpredictable. The bag was, therefore, not inserted into the uterus.

Fortunately we always examine every suspect placenta previa vaginally. We thereby discovered the presence of carcinoma, although unfortunately late in the pregnancy. One of two patients, who had no bleeding at any time, was only diagnosed after an uneventful labor, when a postpartum examination was made.

In preferring a classical cesarean section as a means of interrupting the pregnancy prior to the radiation, we concur with Beck, Titus, McNeil and Schmitz.

Concerning the fetus, it was shown by Strauss that 20 per cent of patients whose cervix was irradiated prior to cesarean section had a microcephalic fetus.

Concerning the fetal salvage, seven mothers had a pregnancy that extended beyond seven months. One died undelivered. One baby died in two days of bronchopneumonia and *B. pyocyaneus* was found in the lung tissues. One was still-born. The four remaining babies had an uneventful course.

ANDROGENIC THERAPY IN MALIGNANT DISEASE OF THE FEMALE GENITALIA*

Preliminary Report

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Introduction

IN AN extensive laboratory study of gonad hormones in 1932, Moore and Price postulated their conception of hormone interactions to include four principles: (1) Gonad hormones stimulate homologous accessories; (2) Secretions produced by the pituitary stimulate the gonads to function both in germ cell production and in hormone secretion; (3) Gonad hormones have no *direct* effect on the gonads of either the same or the opposite sex; (4) Gonad hormones of either sex exert a depressing effect upon the pituitary which results in a diminished amount of the sex-stimulating factor available to the organism.

Although some laboratory work¹⁻⁵ suggestive of a possible gynecogenic effect of testosterone has been reported since the above conceptions were established, most of the work has been confirmatory.⁶⁻¹¹ Salmon¹² after making a comprehensive survey of the literature relative to the effects of androgenic therapy in laboratory animals, points out the contradictory and paradoxical effects obtained by various investigators. He concluded that the application of laboratory results to the human female should be made with caution. After conducting a rather extensive clinical investigation, Salmon has postulated that the therapeutic effectiveness of testosterone propionate in gynecology appears to stem from the following properties: (a) Its ability to inhibit the gonadotropic activity of the hypophysis; (b) to suppress or decrease estrogen production; (c) to nullify or modify the activity of the gynecogens; (d) to inhibit the proliferative processes in the endometrium; and (e) to inhibit the reactivity of the uterine musculature. Thus our clinical concepts, postulated by Salmon and generally accepted today, relative to pituitary and gonad therapy are not dissimilar to the conclusions reached by Moore in his laboratory study.

The urologists have carried these concepts into clinical medicine in their treatment of prostatic carcinomas. It has been well established during the last few years that the estrogens are of definite value in the treatment of carcinoma of the prostate gland. There has been prompt relief of pain and urinary symptoms with regression of prostatic lesions as determined by rectal palpation. There has been, in addition, regression of lymph nodes and of metastatic bone lesions as seen by repeated

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x-rays.¹³ Pathologic studies have revealed actual regressive changes in the cytoplasm and nucleus of tumor cells.¹⁴ These effects are presumedly due to suppression of pituitary function by the estrogenic material which exerts little or no stimulating effects on the male secondary sexual organs. The estrogenic (or androgenic) suppression of pituitary function has been worked out clinically and in the experimental laboratory. In animals both the basal metabolic rate and weight of adrenal glands are decreased by administrations of estrogens. The growth of immature animals is also inhibited. Urinary excretion of the pituitary follicle-stimulating hormone is decreased with administration of estrogens (or androgens).¹⁵⁻¹⁷ Indeed, the rationale of hormone therapy in the menopause is based on the inhibition of the gonadotropic pituitary factor by estrogens (or androgens) when, with progressive ovarian failure, the unopposed action of the gonadotropic hormone produces symptoms.

In the light of these laboratory and clinical studies and in view of the successful application in clinical urology of the conceptions established thereby, an investigation of the possible value of male hormone in the treatment of malignancies of the female genital tract seemed highly warranted. If by the administration of testosterone the depressing effect on the pituitary would diminish the amount of sex-stimulating hormone, and if such administration is without effect upon the heterologous secondary female organs, it seemed not unreasonable to believe that retardation, even possible regression of the malignant growth might occur in a manner comparable to the effect of estrogens on prostatic growths.

A finding of speculative interest in this connection was first pointed out by Asehheim and Zondek, when they found a positive reaction of their pregnancy test in cases of genital malignancy (uterus, ovaries, testes). This has been confirmed by many. No appreciable increase in pituitary gonadotropic factor has been found in the urine in nongenital malignancies and the relationship between the genital growth and the associated increase in urinary gonadotropic hormone in such cases is one of interest. Saphir¹⁸ has postulated that a positive A-Z test in genital malignancy may be due to a destruction of genital function stimulating castration. This hypothesis, however, would seem not to explain satisfactorily the positive reaction obtained in carcinoma of the uterus, where no known destruction of ovarian function has occurred. The possibility that the increase in gonadotropic hormone may be the cause rather than the effect of the genital malignancy suggests itself. If such is the case, administration of testosterone with the resultant depression of pituitary hormone would again seem logical and warranted.

Material and Method

It became apparent immediately that the task of selecting clinical material for such a study was fraught with difficulty. To withhold for experimental purposes any of the accepted modes of treatment to pa-

tients with early carcinoma was, of course, wholly unjustified. Moreover, the administration of testosterone to such patients following surgery or coincidentally with irradiation would make the evaluation of clinical results extremely difficult. We were forced, therefore, to reserve hormone therapy for those patients who failed to respond to orthodox forms of treatment, and for whom it was felt, nothing more could be accomplished. With such criteria for the selection of material, studies were begun on a most discouraging group of patients. Cases were selected from the Northwestern University Clinics and from the private gynecologic service at Passavant Memorial Hospital including carcinomas of the uterine corpus, cervix, Fallopian tube, ovary and breast.

A somewhat generous dose of testosterone propionate was arbitrarily chosen with the thought of "nothing to lose, everything to gain" in these patients. One hundred and forty to 150 mg. weekly were given either as oreton—M, in which case two 10 mg. tablets were taken daily by mouth, or as oreton, in which case the patient received three 50 mg. injections per week intramuscularly.

Case Histories

Our first five patients, including three carcinomas of the cervix and two carcinomas of the corpus, have been receiving testosterone propionate for ten months. During this period, each patient has received more than 6,000 mg. of testosterone propionate intramuscularly. Following is a brief outline of the history and progress of each of the original five patients, with which this preliminary report is chiefly concerned.

CASE 1.—(A. S.) This 39-year-old patient first appeared in the Northwestern University Clinic on November 9, 1939. She had had slight vaginal spotting for one week, and a biopsy done at the Chicago Tumor Clinic had revealed an early carcinoma of the cervix. Five days later, examination under anesthesia at Passavant Hospital revealed an endocervical carcinoma between 8 and 12 o'clock.

Radium was placed intrauterinely in chain tandem and interstitially about the lesion for a total dose of 3,500 mc. hours. The patient developed some necrosis of the cervix, with discharge, vaginitis and rather marked pelvic cellulitis. There was marked induration in the right broad ligament and in the region of the bladder anteriorly. There were some urinary symptoms (frequency, pain, urgency). Cystoscopy and 4 pyelograms revealed edema but no metastases or intrinsic pathology. This cellulitis and induration lasted approximately 9 months (until September, 1940). The first course of x-ray (7,000 r.) was given from 11/20/39 to 2/19/40.

In October, 1940, pelvic examination revealed marked thickening anteriorly to the left and patient was started on a second series of deep x-ray (7,450 r.).

The patient complained of swelling of both lower legs in July, 1941, and in October, 1941, a heavy mass was felt anteriorly and to the left extending to the pelvic wall. Our impression at this time was recurrent carcinoma.

The patient's condition remained stationary and in February, 1942, induration high in the left pelvis was felt with edema of the abdominal wall. This was thought to be the result of gland involvement. Pelvic

examination in May, 1942, revealed persistent induration in the left broad ligament, extending to the ilium. It was nodular.

Examination on January 27, 1943, revealed areas of brawny edema in the left lower quadrant of the abdomen and groin, brawny thickening in the left broad ligament, and a golf ball-sized area of stony hard induration high in the right broad ligament. The cervix was smooth and closed. A third course of deep x-ray therapy (9,000 r.) was given.

On March 10, 1943, rectovaginal examination revealed perirectal nodulations. On 4/7/43 there was edema of both legs and thickening of both broad ligaments.

The first injection was given on 4/9/43. The clitoris began to hypertrophy after a month's treatment, and by 5/19/43 was about four times its original size. Tissues were succulent at this time and have remained so. Vaginal smears have shown moderate cornification.

There has been occasional itching of the skin, but no acne has been manifested. Patient states that her hair is oily and that she has to wash it more often. She began first to notice a beard on May 30, and while it has gradually increased, it is bothersome only on her upper lip. There has also been some increase in leg hair. There have been no breast changes.

During the early part of June, this patient's voice began to deepen and occasionally to crack. This voice change has become progressively more noticeable to both the patient and to us.

Her weight was 218 pounds at the onset of treatment and is now down to 200 pounds. After approximately two months of treatment she became most anxious to lose weight and has been on a voluntary reduction diet since.

On 6/11/43, this patient voluntarily reported that the treatments had markedly increased her sexual desires. She reported an extreme feeling of well-being bordering on euphoria. This increase in libido has been a constant factor. It is still on the increase. Before treatment patient had intercourse once a week or even less, and now has it four times a week. She is wondering whether that is too much.

X-rays of the long bones, skull, and pelvis have revealed no evidence of metastases. Blood chemistry after 6 months' treatment revealed: N.P.N.—36.8; creatinin—1.61; cholesterol—242; calcium—9.1; phosphorus—2.75; phosphatase—4.35; total protein—7.8. Pelvic examination at the end of October, 1943, revealed less broad ligament thickening and the patient seemed to be improved.

CASE 2.—(J. T.) This 60-year-old patient first reported to the Northwestern Clinic in December, 1941. Her history included intermittent vaginal bleeding during the previous three years (15 years after the menopause). These episodes of bleeding were often accompanied by back pain, and did not feel like her menstrual periods previously. Pelvic examination on December 8, 1941, revealed atrophic tissues and a blood tinged vaginal discharge. The cervix was small, smooth, and mobile with a dark bloody ooze coming from the os. The corpus was not outlined on bimanual examination. John Clark test was markedly positive and revealed the canal to be 7 cm. in depth. A diagnosis of carcinoma of the corpus was made and the patient was sent to Passavant Hospital.

On curettage (December 11, 1941), much necrotic, carcinomatous tissue was obtained. Because of the patient's age, obesity, and medical contraindications, radium was chosen in preference to hysterectomy. She received her initial radium treatment on December 11, 1941, a total

dose of 2,800 mc. in the uterine cavity. The microscopic report was adeno-acanthoma of the corpus. Patient received her first course of deep x-ray, a total of 8,350 r. from December, 1941, to March, 1942.

On March 18, 1942, the patient was seen in Northwestern Clinic, complaining of watery discharge. John Clark test was negative. The cervix was open and there was no retained fluid in the uterus. Watery discharge continued and the patient developed lower abdominal discomfort. There was essentially no change in the patient's condition and on July 8, 1942, she was sent to Passavant Hospital for re-evaluation. At this time, a moderate hydropyometria was found with slightly more bleeding than normal. Slight tissue was obtained with occasional suspicious groups of cells seen; no radium was given.

Examinations remained negative during the autumn of 1942, although the patient complained almost constantly of discomfort in the lower abdomen.

On February 2, 1943, curettage at Passavant Memorial Hospital revealed tissue which was definitely adenocarcinomatous on microscopic examination. There was the impression of a friable mass in the right horn of the uterus. A second intrauterine radium treatment was given; the total dose 2,450 mc. hours.

Patient complained of abdominal discomfort during the summer of 1943. She has had broad ligament thickening bilaterally and some obvious necrosis of the cervix presumably the result of radium treatment. Differentiation between extension of the malignant process and post-irradiation reaction has been most difficult in this patient.

Testosterone injections were begun on April 14, 1943. The clitoris has hypertrophied to approximately four times its original size. The vulvo-vaginal tissues have not been particularly succulent. Vaginal smears have shown no estrogenic effect and cells have been characteristic of atrophic vaginal tissues with slight tendency to mucinification.

There have been no changes in the texture of the skin and no breast changes. Slight acneform eruptions appeared on the face at the onset of treatment but soon disappeared and have not recurred. This patient had a tendency toward facial hirsutism prior to treatment and has now developed a marked beard involving the cheeks, chin, and upper lip.

After five weeks of treatment, the patient began to complain of hoarseness. This complaint has been constant and her voice has become progressively deeper.

Her weight at the onset of treatment was 185 pounds, and during the first six months, she gained approximately six pounds. At present, the patient is slightly under her initial weight.

There has been a marked increase in this patient's sexual desires. This increased libido first became noticeable during the last part of May. Prior to treatment, the patient had had no sexual intercourse for two years because she was "too sore." She now has intercourse approximately two times a week and has repeatedly suggested that her husband receive some of the medicine also.

X-rays of the long bones, skull and pelvis have revealed no evidence of metastases. Blood chemistry after six months' treatment revealed: N.P.N.—35.8; creatinin—1.25; calcium—9.6; phosphorus—3.49; phosphatase—2.15; total protein—6.42. There has been much controversy relative to the evaluation of the broad ligament thickening, necrosis, and bleeding which this patient has manifested during the last two months (October and November, 1943). It has been practically impossible to

tell whether the findings in this patient have been on the basis of an extension of her malignancy, or on the basis of postirradiation reaction. While the patient remained cheerful during the first five or six months' treatment, she recently felt somewhat depressed and has had rather severe lower abdominal discomfort.

CASE 3.—(M. B.) This 53-year-old divorcee was first seen by us in the clinic in June, 1936, over seven years ago. She had been having some blood-tinged vaginal discharge with some free bleeding as well. Pelvic examination revealed a large granular cervix which bled easily on examination. The involvement was chiefly of the anterior cervical lip. There was a freely movable bean-size tumor in the vaginal mucosa, one inch below the cervix in the midline. The uterus was retroflexed and of normal size. Attempts to move it were painful. Clinical impression was carcinoma of the cervix. Tissue was taken for biopsy and microscopic examination confirmed our impression of carcinoma. Patient was given 4,000 mc. hr. of radium interstitially in palisade arrangement and in canal. The bean-sized vaginal tumor was also removed. She received a course of deep x-ray (5,000 r.) from July to October, 1936.

Her course was followed in the Gynecological Dispensary and aside from some sloughing of the cervix with discharge was perfectly satisfactory. Pelvic examination on March 3, 1937, showed the cervix to be shrunk and fibrous, with still some watery discharge. There was no infiltration in the broad ligaments or rectovaginal septum. In July, 1937, the impression was one of clinical arrest. There were no complaints referable to the pelvic problem and the patient was followed in the arthritis clinic for some time. Five years after this impression of clinical arrest, the patient developed a Virchow nodule in the left supraclavicular space; biopsy proved it to be squamous cell carcinoma. Impression was then retroperitoneal metastasis. The situation was explained to the patient and arrangements were made to have the services of a local physician.

Testosterone injections were begun on April 14, 1943. Marked hypertrophy of the clitoris was evident by the first of June, and the tissues have been succulent. Vaginal smears are suggestive of mucinification.

After fifteen treatments, the patient began to complain of acne which first appeared on her chest, later on her back. There was only slight facial involvement. The skin involvement has gradually cleared up and has not recurred. A beard was first noted during the first part of June and has increased gradually. It is particularly noticeable on the upper lip and under the chin. Patient has noted no changes relative to the hair on her head but says that there is an increased amount of pubic hair. She has had the impression that her skin has been a trifle drier. There have been no breast changes.

Patient first reported a voice change about the middle of June; it has become progressively deeper since that time.

This patient's weight, approximately 143 pounds at the beginning of treatment, had remained fairly constant until nine weeks ago. Patient has lost eight pounds in the last nine weeks.

Increase in libido was first reported after a month's treatment. It has progressively increased to date. This patient, although not married now, inquired whether or not intercourse would harm her. She felt something must be done about her increased sexual desires.

At the beginning of treatment, this patient was extremely discouraged, but as time went by, she became more and more cheerful. Re-

cently, pain has developed in the extreme lower back and right hip, radiating down the right leg. Bimanual pelvic examination had remained negative until October, 1943, when some suggestion of extension high on the right was discovered. Blood chemistry after six months' treatment revealed: N.P.N.—36.8; creatinin—1.63; calcium—10.3; phosphorus—4.59; phosphatase—2.67; total protein—7.96

During the course of treatment, the metastatic mass in the left supraclavicular region became progressively larger and more painful. Only recently, after x-ray therapy, has there been a marked decrease in the size of this tumor. This patient has maintained her cheerful attitude.

X-rays of the long bones, skull and pelvis taken during the last week in August were reported as negative relative to metastases. After repeat films on November 5 showed obvious metastases, a review of the August films (and also some made in June) revealed the bony involvement to be present all through the series. The metastatic lesions are evidently progressing.

CASE 4.—(R. G.) This 45-year-old patient first reported to the Northwestern University Clinic on October 28, 1942, with complaints of continuous vaginal bleeding of two months' duration and right lower quadrant abdominal pain, which was severe and throbbing in nature.

She gave a history of similar complaints in May, 1939, at which time she was seen in another hospital. A curettage was made on May 14, 1939, and microscopic examination of the curettings revealed adenocarcinoma of the body of the uterus. The patient received two treatments with radium while in the hospital, the total dosage unknown. A course of deep x-ray was given. Following this treatment, the patient was asymptomatic until January, 1942, when she bled for two months. There had been no flow between May, 1939, and January, 1942. A second course of deep x-ray was given. There was no bleeding from March, 1942, to September, 1942, when it again occurred. There was continuous vaginal bleeding from September 1, to her first clinic visit on 10/28/42. The right-sided abdominal pain began again some five weeks prior to this visit. Pelvic examination on 10/28/42 revealed a pelvic mass the size of a 2½ months' pregnancy replacing the uterus with massive infiltration in the base of the right broad ligament and none on the left.

The patient entered Passavant Memorial Hospital the middle of January, 1943, for evaluation. Examination under anesthesia revealed a hopeless recurrence of malignancy with extension into both broad ligaments. Curettings revealed typical adenocarcinoma. Further treatment seemed hopeless and the family was informed of the patient's condition. When seen about a month later in the Northwestern University Clinic, the patient had been bleeding a great deal and there was no change in the degree of pelvic extension, it was extremely marked. Arrangements were made for terminal care.

Definite hypertrophy of the clitoris appeared after five weeks' treatment with testosterone which was begun on April 1, 1943. The clitoris has become roughly four or five times its original size. Tissues have been moderately succulent. Vaginal smears have revealed a picture suggestive of atrophy.

There has been no acne. Skin texture has been unchanged. The patient states that with the onset of treatment, her hair came out in appreciable quantities when combed. This has been less noticeable recently. The patient had developed a beard, particularly marked on her

upper lip. However, facial hirsutism has been of lesser importance here. There have been no breast changes.

Patient began to complain rather strenuously of hoarseness the last part of May, and states that her voice has become progressively deeper since. Voice change has been particularly striking in this patient.

At the onset of treatment, this patient weighed 100 pounds. There has been an increase of weight during the last six months of slightly more than 20 pounds. However, a marked edema of the legs, particularly the right, was present and may be in part responsible for the weight increase.

This patient was quite depressed at the onset of treatment, had no appetite and apparently realized the hopelessness of her condition. The improvement in morale has been striking. She has become increasingly more cheerful and after six to eight weeks of treatment felt well enough to work again. She has found a position and is still working, nine months after terminal arrangements had been made. Although she has not had a husband for some time and had thought nothing of matters of sex for a long time, she offered information relative to her increased libido on interrogation.

X-ray of the long bones, skull and pelvis revealed no evidence of bony metastases. Blood chemistry after six months' treatment revealed: N.P.N.—39.4; creatinin—1.33; cholesterol—2.80; calcium—9.4; phosphorus—3.09; phosphatase—4.96; total protein—7.95.

In November, 1943, pelvic examination revealed no change in the marked induration throughout the pelvis. The edema of the legs, so massive during the last few months, is improved.

CASE 5.—(S. S.) This 49-year-old patient was first seen in the Northwestern Clinic in December, 1932. She was complaining of a bleeding on trauma and between periods, and examination revealed a "precancerous" leucoplakic cervix. Biopsy was recommended but not done. The patient was not seen again until 10/10/34, when she reappeared with a complaint of bleeding daily between periods for two weeks. Biopsy revealed carcinoma of cervix and patient received 4,000 mc. hr. of radium interstitially and into bases of broad ligament by coincident surgical exposure on 11/14/34. Deep x-ray therapy for a total of 5,200 r. was given from December 13, 1934, to February 16, 1935. Broad ligament thickening and cervical obstruction with pyometra resulted. There was also some postradiation cystitis. The induration in the deep right pelvis was very marked through the summer of 1935, and another course of deep x-ray for a total dose of 2,600 r. was given. The process was thought to be extension and the prognosis was given as poor. During the fall and winter of 1935 and 1936 the patient began to improve; she gained weight and the induration gradually decreased. Then on September 2, 1936, there was thought again to be marked extension into the right broad ligament. Another 2,800 r. of deep x-ray was given. On April 7, 1937, there was no further extension and the induration of the right broad ligament was not felt to be advancing.

Pain and edema began to appear in the right leg in August, 1942, and gradually increased. In October, 1942, a one-inch swelling to the right of the cervix between it and the bony pelvis was felt. In March, 1943, stony hard induration was felt between the cervix and the bony pelvis on the right. It was decided to give the patient testosterone because of her poor prognosis.

Treatments were begun in April, 1943. Hypertrophy of the clitoris began after about five weeks' treatment. The organ is now about three

to four times its original size. The vulvovaginal tissues have been less succulent here than in the other patients. Vaginal smears have shown mucinified cells.

During the first two months of treatment, there was some acne on the face and chest. This cleared rapidly and there has been no recurrence. A beard developed after six weeks. The patient at first bleached the hair, but recently has been forced to shave. There has been some increase in leg hair.

The patient has been complaining of voice changes since about the middle of June, 1943. This is particularly marked in the morning. Objectively, her voice is extremely husky and cracks frequently. She states that she can no longer sing.

The patient's weight has been constantly between 170 and 175 pounds.

This patient continues to feel extremely well and except for slight edema of the right leg has no symptoms. She has been considering remarriage for several years, and finally consented after two months' treatment. Libido has been greatly increased.

X-rays of the long bones, pelvis, and skull are all negative. Blood chemistry was as follows after six months' treatment: N.P.N.—37.8; creatinin—1.3; cholesterol—302; calcium—9.3; phosphorus—2.12; phosphatase—2.85; total protein—7.45.

There is little change in the findings on bimanual examination.

Observations and Discussion

The final evaluation of a study such as we have undertaken requires much time. The clinical course of each patient must be observed carefully for a long period and must be followed up by any pathologic data which may ultimately become available. Because the final chapter in each case may not be written for some time, and because of the several interesting clinical observations already made during the course of treatment, this preliminary report seemed merited. This initial report deals primarily with our five original patients although occasional reference to subsequent patients is made.

Among the early changes noted were those manifested in the vulvovaginal tissues. A constant finding in our original group, and one which has been observed in most but not all of our subsequent cases has been hypertrophy of the clitoris. This observation has frequently been reported by others during therapy with testosterone when the dose has exceeded 250 to 350 mg. per month. Enlargement of the clitoris in our patients who have received slightly in excess of 600 mg. per month has been observed to begin after about four or five weeks of therapy and has progressed until in most cases the organ has reached up to four times its original size.

In most cases the tissues have remained somewhat succulent and appear somewhat engorged. They are not atrophic as one might expect in patients who have received large doses of x-ray and radium.

The reports in the literature relative to the effect of male hormone therapy on the vagina as evidenced by the vaginal smear are conflicting. Deanesly and Parkes⁵ in 1936, working with immature, ovariectomized,

and adrenalectomized rats concluded that testosterone had a direct effect on the vagina manifested by opening of the canal with cornification. Nathanson and Towne¹⁵ noted a profuse vaginal discharge in four patients following injections of testosterone and found that the discharge consisted in part of cornified cells. All four patients showed an estrogenic effect on the vaginal smears. Two had complete cornification. However, other workers, working together and independently have reported a transition to an atrophic, menopausal type of smear following large doses of testosterone. There was a gradual replacement of the usual large squamous epithelial cell types characteristic of the normal cycle by smaller, rounder, and more compact cells with large, well-preserved nuclei.¹⁹⁻²²

In only one of our patients (Case 1, A. S.) has there been any evidence of cornification. The estrogenic effect in this case was moderate and vaginal smears have changed very little since treatment was instituted. Vaginal smears made on the remainder of our original group have consistently shown small, round cells with large nuclei similar to those reported by Papanicolaou, Ripley, and Shorr.¹⁹ The picture has been varied between mucinification and atrophy.

In his discussion of androgenic therapy in gynecology, Salmon,¹² after amplifying his initial studies, concluded that the vaginal smear effects varied with the dose of testosterone propionate administered. In his group an estrogenic type of smear was obtained only when concentrated courses (50 to 100 mg. per day) of testosterone propionate were administered for at least three weeks. Even 25 mg. dose daily for many months did not produce this estrogenic-like action. This concept perhaps explains the varied results obtained by different investigators and certainly is consistent with our findings.

A beard has appeared in nearly all our patients in from four to six weeks and has become increasingly more marked with continued treatment. Although, at first, in some cases bleaching sufficed to minimize the unfavorable appearance caused by this facial hirsutism, all of our original patients have resorted to using a razor. There has been some increase in the amount of hair on the legs in two cases and in one patient the amount and extent of pubic hair has definitely increased. Although one patient reported early in the course of treatment that her hair was falling out in large quantities on combing, this soon ceased and all in all there have been no remarkable changes in the cranial hair.

Three of our original five patients complained of acneform eruptions during the first two months of treatment. These eruptions appeared on the chest, back, and face. Although bothersome to the patient, this condition has been transient in each case and has occurred in many of our subsequent patients. Generalized itching has occurred from time to time in one patient, but skin changes have otherwise been negligible. No breast changes have been observed.

One of the most striking manifestations of treatment and one of the most distressing to the patient has been change in voice. This first began to appear in from four to six weeks, concomitantly with the enlargement of the clitoris and appearance of a beard. In some instances, the voice has become quite masculine in depth and in most cases has become harsh and rasping in quality, cracking frequently in the course of conversation. This hoarseness, as the patient subjectively describes it, has been perhaps the most bothersome of the undesirable side effects noted in the course of treatment.

Probably the most encouraging observation noted in our group early in the course of treatment has been improvement of morale. There has been a definite feeling of well-being bordering at times on euphoria. There has been a marked change in mental outlook, for the most part, from one of hopelessness prior to injections to one of cheerfulness. It has been recognized for some time that symptoms of the menopause can be controlled by administration of androgens and this may be in part the explanation for the improvement seen in these patients in whom menopause has been induced by radium and x-ray. Certainly less fatigue, less nervousness, and in most cases fewer flushes were noted after injections were under way.

Associated with the progressively increased feeling of well-being has been a definite and consistent increase in libido. This has been constant in our original group and in essentially all of our subsequent cases. It has been marked enough in most instances to elicit voluntary information from the patients relative to matters of intercourse. For instance, Case 1 (A. S.) has increased the number of times she has intercourse per week from one to four and has asked if more would be harmful; Case 2 (J. T.) has resumed intercourse after a 2-year lapse, is having relations twice a week, and has several times inquired as to the possibility of her husband receiving injections; Case 3 (M. B.), although no longer living with her husband, has asked whether or not intercourse would harm her because her sexual desires have become intolerable; Case 5 (S. S.) had been considering remarriage for several years, and finally wedded after two months' treatment, acknowledging a marked increase in her sexual desires; Case 4 (R. G.), although not voluntarily offering any information, readily admitted on direct questioning, her libido was increased.

These observations were of particular interest to us in the light of conflicting reports in the literature. Salmon,¹² in his fore-mentioned study, reported that many of his patients experienced a definite increase in libido during the course of injections and for several weeks thereafter. The majority of his cases received more than 500 mg. of the hormone in one month. The clitoris in many of these women became hyperemic and very sensitive to touch. These results were essentially the same as in our group. Greenblatt, Mortara, and Torpin,²³ using pellet im-

plantation of testosterone propionate in varying dosage, likewise reported a resurgence of libido in almost every one of 55 patients, who once had had normal sexual desires.

However, Silberman, Radman, and Abarbanel,²⁴ using smaller doses of 5 mg. two to three times per week, were able to control menopausal symptoms in 15 patients, but noted no change in libido. Interestingly enough, Rubenstein, Shapiro and Freeman²⁵ have reported successful relief in five women suffering from abnormally strong sexual desires by the administration of 25 mg. of testosterone propionate at varying intervals. Since the exaggerated sex urge in these patient was definitely associated with premenstrual tension and since such tension has been successfully treated by testosterone propionate, relief may have been on this basis. However this may be, there is certainly no question as to the increase in libido in our group.

Particularly worthy of emphasis among our observations are: (1) feeling of well-being approaching euphoria at times, (2) improved appetite (some of our subsequent patients have notably gained weight), (3) control of menopausal symptoms (viz., depression, nervousness, insomnia, and to a lesser degree flushes), and (4) increased libido. These findings have been consistent and gratifying and of themselves seemingly justify our efforts. The masculinizing effects of our large doses of testosterone have been definite, but in most instances readily accepted by the patient as secondary to her improved physical and mental well-being. The realization that something is being done for them coupled with subjective improvement has apparently minimized the untoward masculinizing symptoms, and has offered new hope to these unfortunate patients. Their cooperation and faithfulness in keeping appointments have been truly remarkable.

On the other hand, there is nothing to indicate that there has been any regression of the malignant process in any case. Indeed, in one case (Case 3, M. B.), there is definite evidence that the growth has progressed during treatment. The metastatic supraclavicular mass became increasingly larger until x-ray was given and repeated x-rays of the long bones have shown progression of the bony metastases during the last five months. Although it is true that the remainder of our original group (particularly Case 4, R. G.) have done well in the light of their prognosis prior to the onset of treatment, any retarding effect on the cancerous growth remains unestablished. The effect of treatment upon the malignant process will be difficult to evaluate, will require much time, and should include the study of any pathologic data which may ultimately become available.

Varying the dosage of testosterone seems indicated. It is possible that the desirable symptomatic results above described may be obtained with a smaller dosage which would eliminate the masculinizing effects. This is being done in some of our subsequent patients.

Summary

A series of patients with previously treated but progressively advancing malignancies of the female genitalia have been given testosterone propionate in arbitrary dosage of 140 to 150 mg. weekly. Cases include carcinomas of the breast, ovary, Fallopian tube, uterine corpus and cervix. A preliminary report of five cases in detail including carcinomas of the uterine corpus and cervix is presented. These patients have been receiving treatment for ten months. A theoretical consideration of the basis for this clinical investigation is given and our observations noted. Symptomatically, these patients have been definitely improved. Feeling of well-being, improved morale, control of menopausal symptoms, and increased libido have all been regularly observed and these observations alone seemed to us to warrant the administration of male hormone in this unfortunate group of patients. To date, there is nothing to indicate any regression or even retardation of the malignant process.

Conclusions

1. All our patients have shown striking improvement in morale with feeling of well-being bordering at times on euphoria.

2. There has been a definite improvement of menopausal symptoms such as nervousness, insomnia, headache, depression, and, in most cases, hot flashes.

3. Increased libido has been consistent and marked.

4. With our arbitrary dosage (140 to 150 mg. per week) masculinizing symptoms have appeared in all patients and have included hypertrophy of the clitoris, development of a beard, and voice change. Acne-form eruptions have occurred in three of our original five patients and in many of subsequent cases.

5. Vaginal smears have tended toward the atrophic state and have changed little during treatment. In one patient some suggestion of cornification was seen from the beginning.

6. To date, there is nothing to indicate any regression or even retardation of the malignant process in manner comparable to the effect obtained in estrogenic treatment of prostatic carcinomas. In one of our original patients and in two subsequent cases, metastatic lesions have been seen to progress during the course of treatment (one carcinoma of cervix and two carcinomas of breast).*

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References

1. Salmon, U. J.: *Endocrinology* 23: 779, 1938.
2. Nelson, W. O., and Gallagher, T.: *Science* 84: 230, 1936.
3. Nathanson, I. T., Franseen, C. C., and Sweeney, A. R.: *Proc. Soc. Exper. Biol. & Med.* 39: 385, 1938.

*Work is being continued.

4. Salmon, U. J.: *Proc. Soc. Exper. Biol. & Med.* 38: 352, 1938.
5. Deanesly, R., and Parkes, A. S.: *Brit. M. J.* 1: 257, 1936.
6. Rubenstein, H. S., and Solomon, M. L.: *Endocrinology* 28: 112, 1941.
7. Rubenstein, H. S., Kurland, A. A., and Goodwin, M.: *Endocrinology* 25: 724, 1939.
8. Hamilton, J. B., and Wolfe, J. M.: *Endocrinology* 22: 360, 1938.
9. Mazer, M., and Mazer, C.: *Endocrinology* 24: 175, 1939.
10. Browman, L.: *Proc. Soc. Exper. Biol. & Med.* 36: 205, 1937.
11. Robson, J. M.: *Proc. Soc. Exper. Biol. & Med.* 35: 49, 1936.
12. Salmon, U. J.: *J. Clin. Endocrinol.* 1: 162, 1941.
13. Kahle, P. J., Ogden, H. D., and Getzoff, P. L.: *J. Urol.* 48: 83, 1942.
14. Schenken, J. R., Burns, E. L., and Kahle, P. J.: *J. Urol.* 48: 99, 1942.
15. Nathanson, I. T., and Towne, L. E.: *Endocrinology* 25: 754, 1939.
16. Rothermich, N. O., and Foltz, L. M.: *Endocrinology* 27: 37, 1940.
17. Salmon, U. J.: *Proc. Soc. Exper. Biol. & Med.* 37: 488, 1937-1938.
18. Saphir, W.: *Endocrinology* 18: 191, 1934.
19. Papanicolaou, G. N., Ripley, H. S., and Shorr, E.: *Endocrinology* 24: 339, 1939.
20. Rothermich, N. O.: *Endocrinology* 25: 520, 1939.
21. Papanicolaou, G. N., Ripley, H. S., and Shorr, E.: *Proc. Soc. Exper. Biol. & Med.* 37: 689, 1937-1938.
22. Shorr, E., Papanicolaou, G. N., and Stimmel, B. F.: *Proc. Soc. Exper. Biol. & Med.* 38: 759, 1938.
23. Greenblatt, R. B., Mortara, F., and Torpin, R.: *AM. J. OBST. & GYNEC.* 44: 658, 1942.
24. Silberman, D., Radman, H. M., and Abarbanel, A. R.: *AM. J. OBST. & GYNEC.* 39: 332, 1940.
25. Rubenstein, H. S., Shapiro, H. D., and Freeman, W.: *Am. J. Psychiat.* 97: 703, 1940.

Discussion

DR. ARTHUR H. CURTIS.—I have used, and have been greatly impressed with the therapeutic activity of the male sex hormone, testosterone propionate, since it first became available for use, some years ago. Please note that I say "therapeutic activity" rather than "therapeutic value," for the latter expression must still be held in abeyance.

We have long known that Perandren (Ciba), Oreton (Schering) or the same product manufactured by other houses, is potent in control of menstrual bleeding. Its dependability is limited to that menstrual period during which it is administered, but any product which suffices for temporary control of hemorrhage is a valuable aid in furthering permanent relief. Again, the male hormone eases the menstrual molimen, and now that the hormone is available in the form of orally administered tablets, it is a medicament of real value in selected cases.

The usefulness of testosterone propionate in the relief of angina pectoris has been verified by many observers. Here, its value is probably ascribable to the production of prolonged vasodilatation. In older men, in selected cases and with carefully adjusted dosage, the sense of well-being obtained, the disappearance of fatigue, the resurgence of youthful vigor and the return of youthful emotions are worthy of more than passing note.

I have become almost converted to the belief that estrogens, even in therapeutically modest dosage, are a definite menace to many women because of their carcinogenic influence. I avoid estrogens not only in those cases in which they cause bleeding, but also in all cases with extensive endometriosis, or adenomyosis of the rectovaginal septum, and in all those who have been operated on or irradiated for carcinoma. In these cases, the male hormone finds its field of greatest promise.

For relief of patients with refractory menopausal symptoms small amounts of testosterone propionate may be used in conjunction with estrogens, or independently. Strangely enough, although other symptoms are thereby commonly alleviated, the flashes tend to persist; in fact they may be made worse, even by modest oral dosage.

My experience with the male hormone in cancer cases, limited entirely to oral administration, parallels that of Dr. Abel. Contrary to the usual story in patients with malignancy, euphoria is a dominant feature. My patients have not had hypertrophy of the clitoris, nor have they been annoyed by inordinate sexual appetite. Hypertrichosis, however, has been more marked than in those younger women to whom we formerly administered somewhat less perandren parenterally for relief of menorrhagia. I assume that the considerably older age of cancer patients and the continuous administration of the hormone are factors. Regarding the effect on the cancerous growths it would appear at this premature time that the male hormone is an excellent palliative remedy, perhaps comparable with the helpfulness of palliative irradiation. Several cases in which I would have expected an early return of the growth have remained in a state of clinical arrest for a surprising period of time. When once the growth begins to recur, the hormone appears to be unavailing in arresting its progress.

DR. PHILIP F. SCHNEIDER.—This preliminary report on androgen therapy in malignancy of the female genitalia is of considerable interest regardless of the fact that no regression of tumor growth has been observed. The clinical improvement which has been reported in each patient, particularly in view of the advanced stage of the carcinoma, seems to justify the use of these substances and provides a method for further study of the relationship of the endocrines and carcinoma.

The conflicting reports in the literature regarding the results obtained with endocrine substances can usually be explained to some extent by the dosages employed. In the use of insulin, for example, the importance of accurate dosage is clearly demonstrated not only clinically but by means of blood sugar determinations. It is known that the nearest approach to the true physiologic normal can be obtained only by exact controlled dosage, while the administration of excessive or deficient amounts of insulin always produces abnormal physiologic effect.

In a considerable experience with estrogenic substances in the treatment of menstrual and obstetrical disorders due to estrogenic deficiency and in treatment of the menopause, similar observations have been made. The same symptoms and effects which are due to an estrogenic deficiency can be produced in the same patient by the administration of excessive amounts of estrogenic substance, while the nearest approach to the normal physiologic condition, both subjectively and objectively, can be obtained only by administration of the exact amounts necessary to compensate for the individual deficiency. This point is also demonstrated by our experience with the synthetic estrogenic preparation, stilbestrol. In our early experience with this substance the nausea, vomiting and bleeding accompanying its use were first attributed to a toxic effect of the substance itself. Subsequent experience has revealed that these so-called toxic effects were merely the results of overdosage. It seems logical to conclude that similar abnormal reactions may occur in the use of androgenic substances as is evident in all of the cases reported. The masculinizing effects and the occurrence of excessive libido which have been encountered in each of the five cases must be considered abnormal physiologic effects due to overdosage. It seems likely that with individualized dosage, which in this instance could be described as the maximum dosage possible in each instance, which would fall just short of producing the abnormal physiologic effects described could be expected to produce the maximum beneficial effect as far as tumor growth is concerned if any such beneficial effect is possible. The authors have made no statements as to the effect of androgenic therapy on bleeding which was present in any of the five cases when androgenic therapy was instituted. It would be interesting to know what their experience has been.

DR. EDWARD ALLEN.—Some months ago we began to look for suitable cases for this type of therapy. We felt in the beginning if any tumor were to be affected by androgenic therapy it should be an ovarian tumor. While waiting for such

cases to appear, we obtained four cases of carcinoma of the cervix. Rather large doses over a considerable period of time gave the same general effect as Dr. Abel described, but no effect on the symptomatology or changes in growth.

We then found three ovarian carcinomas that seemed to us to be in the right age group and with such extensive involvement that we could evaluate the relief of symptoms. One was a young woman of 27, one was 38 and one was 51 years of age. We taught these patients to take their hypodermics of perandren.

One case was so extensive that we felt justified in withholding any other type of therapy, while the other two were given x-ray therapy. The one receiving no x-ray is now dead of a generalized carcinomatosis. She had had a bowel obstruction for which she was operated upon twice. At the pulmonary operation, carcinoma was found spread all over the abdomen, but she had no visible growths at the time of the second operation. All three patients developed hirsutism but none showed appreciable changes in the clitoris. We did not question these patients specifically about their libido, but the two married ones did speak voluntarily of a marked increase. None of them gave evidence of or complained of menopausal symptoms.

One of the patients treated also by x-ray had undergone two operations, the first being done for the removal of one ovary only, no carcinoma being present or at least no diagnosis being made at that time. The second operation completed the castration and removed the uterus, x-ray therapy being subsequently given. When we first saw her, this patient had marked edema of the legs but at the end of a month, and a half on androgenic therapy, this edema had all disappeared. She felt very much better and she is back at work. The last time I saw her she had what you might call euphoria, and, though she has hard nodular masses all over the left side of the abdominal wall, she appears to be a healthy woman.

The last case had been sent to Chicago to a general surgeon for excision of a tumor of the navel which had been treated by applications of silver nitrate by a physician who had not been aware that she had this huge tumor in the pelvis. The ovaries were removed but the uterus left in on account of its fixation in the pelvis by carcinoma. She gained fifteen pounds after the operation although she had masses of microscopic carcinoma that I believed would kill her in a short time. That is a year and a half ago and she is now getting discouraged with no longer any feeling of well-being. The androgenic therapy did not stop the growth of the tumor, but I do feel that all three of these patients lived longer than under ordinary circumstances and felt better during this time.

DR. ARTHUR H. CURTIS.—Two of the few cases that I followed had the following: one a primary growth which originated either in the tube or in the ovary, and the other, an extensive malignant granulosa cell tumor of the ovary. This is rather interesting in view of Dr. Allen's comments. Both of those are getting along very nicely.

DR. ABEL (closing).—I would like to amplify a little our report on the question of bleeding. Our original five patients had had either x-ray or radium, so that the menopause had been previously induced, and none had bleeding at the time of treatment. There were two cases of carcinoma of the breast, however, which were having menses at the time treatment was instituted. Menstrual periods stopped promptly in each case.

Relative to voice change, there is one other point of interest. In two of our original five patients, the vocal cords were edematous and pale on laryngoscopic examination. That was about the only change observed.

DEVELOPMENT AND DEGENERATION OF OVUM AND FOLLICLE AS OBSERVED BY INTRAVITAL STAINING*

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A CORRECT understanding of any organ is based upon the study of its anatomy and the study of its physiology. The anatomic approach consists of macroscopic and microscopic findings obtained after the death of the organ. The physiologic approach consists of animal experiments and chemical reactions during life.

The anatomic, especially histologic, approach has the advantage of providing readable pictures which stand before us as facts. It has the disadvantage that such illustrations demonstrate the structure, not the function.

The physiologic approach has the advantage of dealing with living tissue. It has the disadvantage that its findings are open to divergent interpretation.

Both methods are limited insofar as the ovary is concerned. Further progress is attained by combining both methods.

An example of such combination which proved to be of practical value is the use of endometrial biopsy as a mirror of ovarian function.

Another combination is the use of vital staining instead of postmortem staining. Dyes known by their physical and chemical properties, injected during lifetime, provide histologic pictures which tell us how organisms or individual tissues deal with or respond to these substances. Such method, therefore, throws light on certain unsolved problems.

As far as the ovary is concerned, the use of vital staining has been limited and not very successful. The reason is that these organs are as well protected chemically as they are physically.

It has been our endeavor to observe the development and degeneration of follicle and ovum under the influence of intravital staining, and to have seen whether or not new information could be obtained in regard to any of the numerous problems hitherto unsolved.

Definition of Vital Staining

“Vital staining” can be defined as the injection of dyes into the living organism and the resultant staining of living tissues. “Supravital staining” is the term used when the tissues are removed first from the living organism and immediately stained afterward. The term “Supravital staining” should also be used when the stain is injected during life,

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but causes the death of the organism. "Intravital staining" is the method which is applied during lifetime, without causing death or lasting damage to the organism.

We shall see later that by microscopic examination, we can easily differentiate between intravital and supravital stained tissues and cells.

Dyes for vital staining can be injected intravenously, intramuscularly, intraperitoneally, subcutaneously, etc.

History of Vital Staining

The history of vital staining covers a period of about seventy years. There have been two distinct phases.

The first phase consists of the injection of dyes and the observation of how they were eliminated by the organism. Thus, the functions of kidneys, liver, salivary glands etc., were studied (Heidenhain,¹ Krause²).

The second phase is interested in the storage of dyes within the organism (Aschoff,³ Moellendorff⁴ and co-workers). It has been found that the reticulo-endothelial system plays a leading role in this process.

Acid dyes are less toxic because they invade primarily connective tissue. Alkaline dyes are more toxic because they have no selective affinity and invade almost any type of tissue. Some dyes stain by diffusion (true staining), others are stored as granules. Those which stain by diffusion are eliminated rapidly. Those which are found as granules are stored over a longer period. The storage takes place in the cytoplasm. The living nucleus never takes any stain.

Parenchymatous and epithelial cells do not take any stain. Exceptions are those organs which eliminate the dye. The material which is injected into the blood stream is first deposited in the least important parts of the body, the connective tissue. From here it is transferred to the kidneys, salivary glands, intestines and liver for elimination.

The most important organs of the organism, the central nervous system and the reproductive glands, are best protected against invasion and therefore, hard to attack by vital staining.

History of Vital Staining of the Ovary

Vital staining of the ovaries has been undertaken almost exclusively with dyes which are stored as granules. Borell,⁵ a co-worker of Aschoff, observed the storage of lithium carmine in the granulosa of degenerating follicles. Goldmann⁶ observed the presence of dye granules also in the granulosa of growing follicles. Eisler,⁷ a co-worker of von Moellendorff, reported the occurrence of trypan blue in growing as well as degenerating follicles. Italian authors succeeded in staining the connective tissue of the ovary.

To force staining compounds into the ovum itself within the living ovary has not been achieved as far as we could ascertain from the litera-

ture. It has been our endeavor to fill this gap. The ovum is the very center of the reproductive female organs. To accomplish this seemed to promise broadening of our knowledge in various directions.

Method and Material

Success or failure of our experiments depends upon the choice of the dye and the choice of the animal. So far as the stain is concerned, the following conditions have had to be fulfilled:

1. The dye has to be acid, water-soluble and not fat-soluble. Alkaline and fat-soluble compounds are toxic.

2. The dye has to have the property of fast diffusion, in order to invade tissues otherwise not approachable.

3. Dyes with the tendency to be stored as granules could be more or less discarded, since their almost exclusive use in the hands of experienced workers has not achieved the vital staining of the ovum proper.

Indigo carmine fulfills the conditions afore-mentioned. We used a 2 per cent solution. In a few instances, trypan blue and neutral red were used.

So far as the animal is concerned, the following conditions have had to be fulfilled:

1. The animal has to have sufficient size to permit intravenous infusion of the stain by the drip method.

2. The animal has to have sufficient power of resistance to withstand a general anesthesia over a long period, and then a laparotomy.

3. The animal has to have ovaries of satisfactory size and a sufficient number of active, i.e., growing and degenerating follicles.

The common house cat fulfills the conditions outlined. We used twelve 1- to 2-year-old females and one male. Ten cats received 2 per cent indigo carmine in increasing doses from 50 c.c. to 600 c.c. intravenously. Best results were obtained with the 200 c.c. dosage (intravital group). Larger amounts caused circulatory damage and death (supravital group).

One cat received 150 c.c. of 0.5 per cent trypan blue, 1 cat 90 c.c. of neutral red. The male cat was used to give us an opportunity to study the male sex glands by the use of vital staining. One cat was pregnant and gave us an opportunity to study the uterus, placenta, fetus, and the amniotic fluid.

Indigo carmine and trypan blue gave similar results so far as the ovary was concerned. We would like to point out, however, that the elimination of these compounds through the kidneys takes place in opposite ways.

Indigo carmine is eliminated through the tubules (Fig. 1), while the glomeruli show no stain. Trypan blue is eliminated through the glomeruli (Fig. 2), while the tubules are entirely inactive. The elimination of trypan blue is considerably slower than that of indigo carmine. The latter diffuses more rapidly into the tissues. Both principles were helpful in our work.

Neutral red is toxic because it invades all tissues. For our experiments, it proved to be of no value. In all instances of intravital staining, it was impressive to see the entire animal turn blue and still act normally after regaining consciousness from the anesthesia.

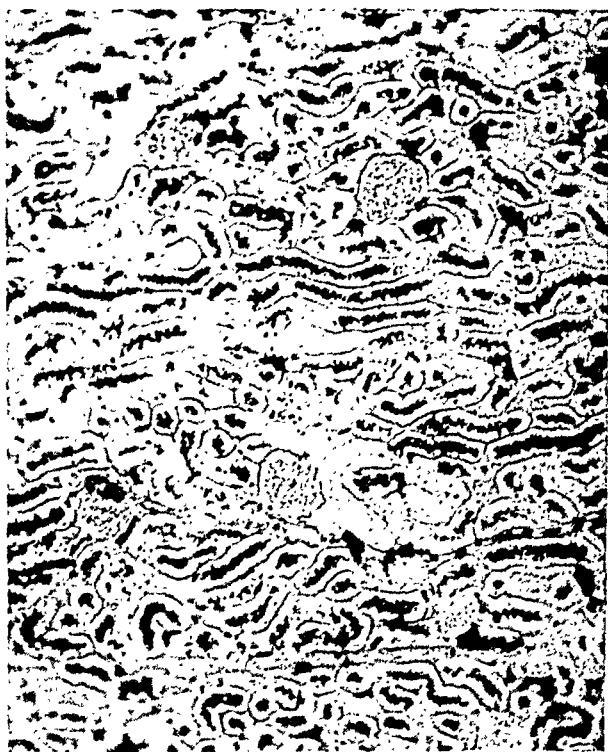


Fig. 1.—Kidney intravitaly stained with indigo carmine. The dye is in the tubules only. No dye in the glomeruli.

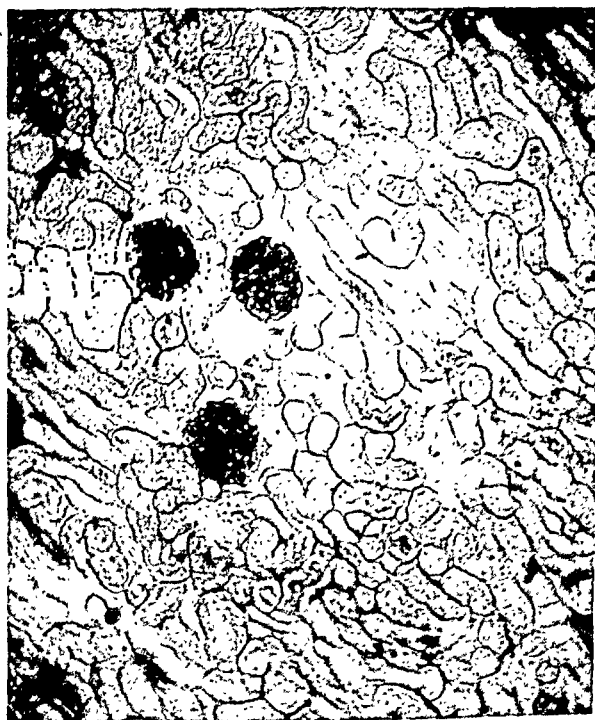


Fig. 2.—Kidney intravitaly stained with trypan blue. The dye is in the glomeruli only. No dye in the tubules.

The ovaries, tubes and uteri were removed at laparotomy. We also studied all other inner organs in some of the animals. We limit this report to the observations on the ovaries.

The removed organs were rapidly dehydrated, fixed and finally embedded in such a way, that any loss or diffusion of the intravitaly applied stain was avoided. Serial sections were made from all ovaries. Every other section was counterstained by different methods. The odd numbered sections received no counterstain and showed the vital stain only.

(Exact details of material and technique are published elsewhere.⁸)

Observations on Ovum and Follicles

A picture of an intravitaly stained ovary under low power shows the albuginea to be blue but the primordial follicles colorless. The growing follicle is partly blue, partly without stain. High power gives us more detailed information.



Fig. 3.—Ovarian cortex intravitaly stained. Primordial follicles near albuginea without stain. Collapsed, degenerated follicle in stroma stained.

Figs. 3 to 12 are black and white reproductions from colored slides. The dark areas represent the blue vital stain as described in the paper and observed in the original microscopic sections.

Primordial Follicles

Under high power, we see the cardinal difference between primordial follicles in the resting stage and those which are degenerated (Fig. 3). Living primordial follicles do not take any vital stain. Degenerated primordial follicles are deeply stained. In other words, living primordial follicles, representing the most valuable building material of the ovary, are exceptionally well protected and at the same time excluded from

the circulation of blood and lymph stream. Degenerated follicles, on the other hand, are useless and therefore, the ideal place to deposit harmful foreign material such as the stains. They take the stain, even if the surrounding stroma remain untinged. They can also be recognized by the collapsed outline of the ovum.

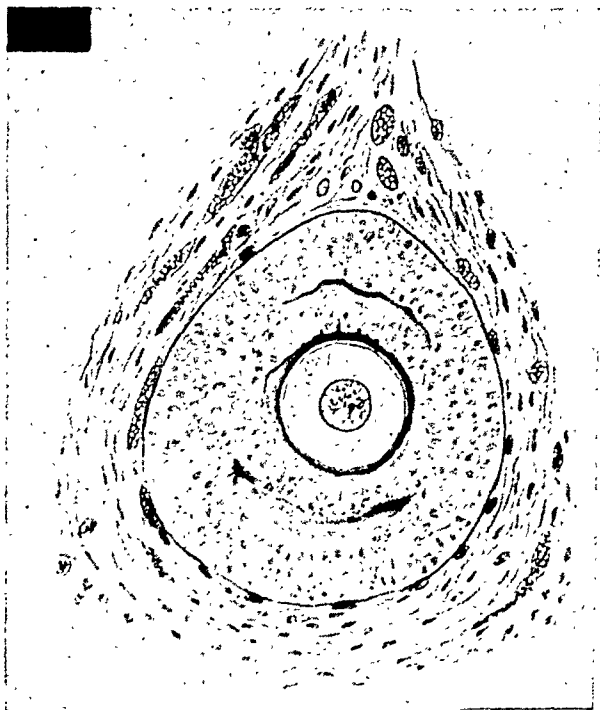


Fig. 4.—Small Graafian follicle intravitaly stained. The dye is found in the zona pellucida of the ovum and in the liquor folliculi.

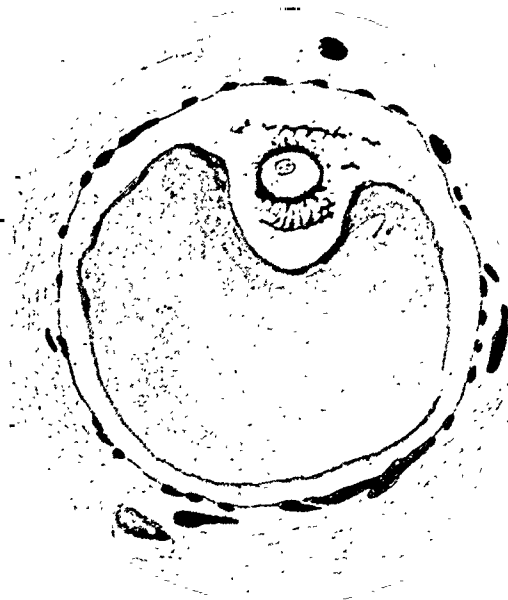


Fig. 5.—Large Graafian follicle intravitaly stained. Dye is present in zona pellucida, liquor folliculi and surrounding blood vessels.

The Growing Follicle

The growing or Graafian follicle responds in a very typical way to intravital staining. We always find the material at two places, in the liquor and at the zona pellucida of the ovum. The inside of the ovum

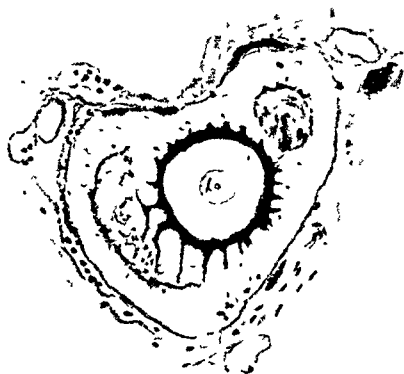


Fig. 6.—Supravitaly stained small Graafian follicle. Intensified staining of zona pellucida, liquor and blood vessels. Appearance of dye in nucleus of ovum.

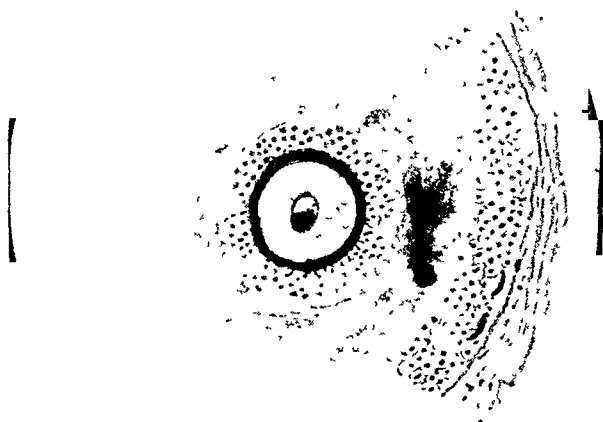


Fig. 7.—Supravitaly stained ovum of large Graafian follicle. Dye in nucleus and zona pellucida.

and the granulosa cells remains colorless. Fig. 4 demonstrates these facts in a small Graafian follicle. Here the liquor formation is just beginning in both poles. This follicle, by the way, shows also the theca interna cone which we described in previous publications. Fig. 5 represents a large Graafian follicle. Here, again, the zona pellucida surrounding the ovum is deeply stained. There is also considerable staining of the liquor especially in the neighborhood of the cumulus ovigerus, indicating that this part of the follicle is the center of circulatory supply. There is one degenerated primordial follicle deeply stained in the adjacent stroma.

By increasing the amount of dye to the point of the animal's death (supravital staining), we obtain the same features only more intensified. (Fig. 6.) The zona pellucida shows a blue double contour. The intercellular spaces between ovum and liquor in the corona radiata become visible. In addition, crystallized indigo carmine is present in the blood vessels, which is a sure sign of circulatory failure or death of the animal.

Fig. 7 demonstrates the ovum of a large Graafian follicle by supravital stain. The nucleus has taken up the stain, indicating the death of the ovum proper. The nucleus in the living ovum under intravital staining remains colorless. The ovum is the most sensitive cell in the follicle and the first one to die. The granulosa cells in Fig. 7 are still alive as indicated by their lack of blue stain.

Death is a slow process. Vital staining is a good method to study the progress of dying in the individual elements of the Graafian follicle. There is an important difference in the picture we obtain in ovaries when the animal dies and the Graafian follicles die with it on the one hand, and when the follicle degenerates in a living animal on the other hand.

Degenerating Ova and Follicles

The degeneration of a follicle begins in the ovum. Vital staining is a method to detect the onset of degeneration at a time when no change of form or structure is visible.

Fig. 8 represents a small growing follicle with beginning degeneration. The ovum is flooded with blue material. The nucleus is darkest. The granulosa cells are stainless, therefore, still alive. There is no zona pellucida in the ovum of small follicles.

When degeneration progresses in small follicles, the ovum loses its round form and collapses. The granulosa cells disappear by absorption (Fig. 9).

An important fact is revealed by these pictures. The ovum governs the follicle. Degeneration of the follicle begins in the center or nucleus of the ovum, progresses to the ooplasm and finally leads to the destruction of the granulosa.

The degeneration of large follicles takes place in a similar way. The only difference is caused by the zona pellucida, which prevents the flooding of the entire ovum at one time. Infusion of the stain takes place where the zona is already weakened. Where the double contour indicates that the zona is still intact, we find the adjacent ooplasm unstained. (Fig. 10.)

As afore-mentioned, the degeneration of the granulosa cells does not coincide with or precede that of the ovum. It is the ovum which causes the degeneration of the granulosa cells. In larger follicles, this process begins at the inner layers adjacent to the liquor (Fig. 11.)

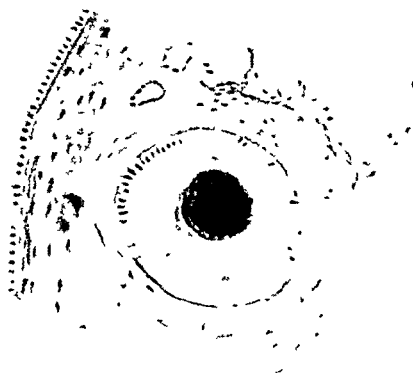


Fig. 8.—Beginning degeneration in small follicle, intravitaly stained. Entire ovum, nucleus and ooplasm flooded with dye.

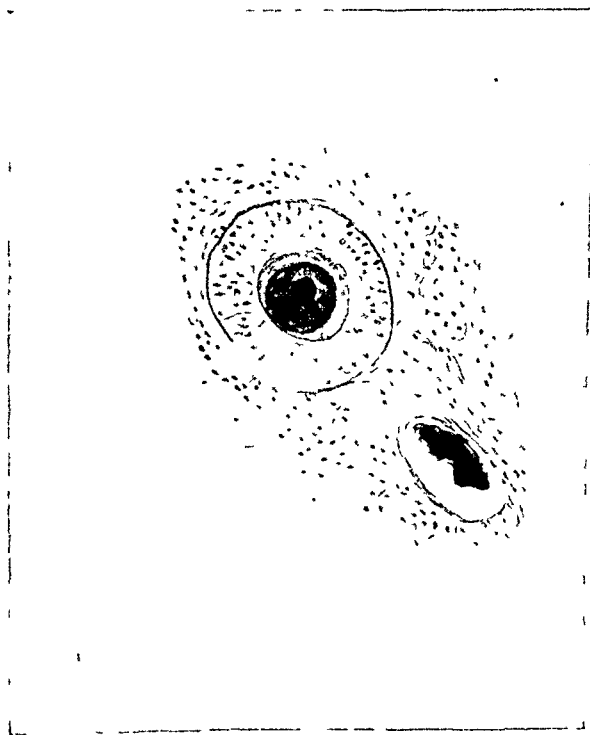


Fig. 9.—Progressing degeneration of two small follicles. Ovum flooded with intravital dye. Granulosa in one follicle absorbed.

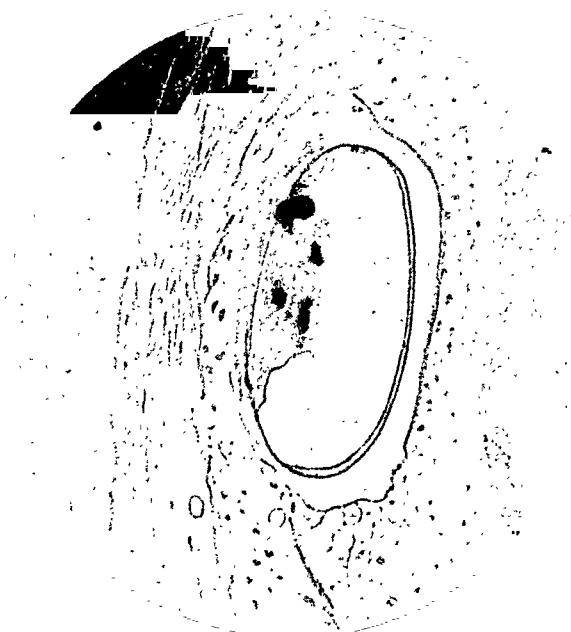


Fig. 10.—Large follicle in degeneration. Ovum partly filled with stain. Nucleus stained.

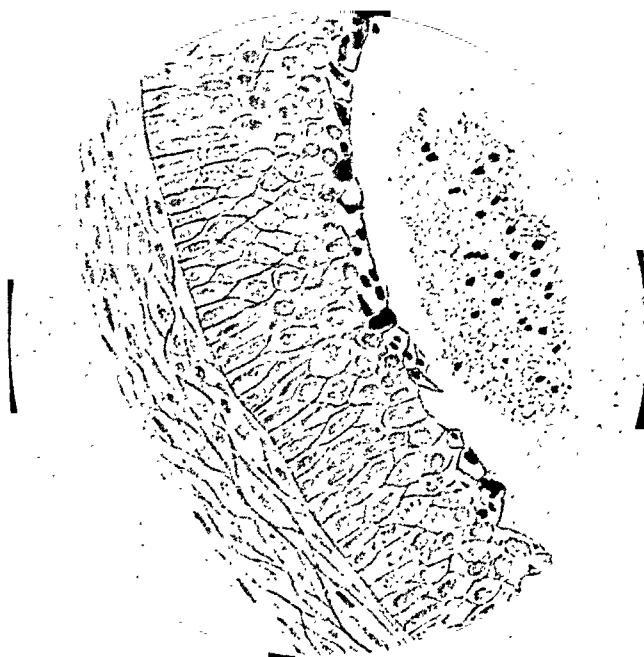


Fig. 11.—Large follicle. Beginning degeneration of granulosa. Dye present in inner layers and in chromatin droplets in liquor from broken-down granulosa cells.

The innermost layers of granulosa cells take up the stain, while the outer layers are still without color.

Finally, the outer layers also succumb. There is a difference in various parts of the follicular wall. The sectors close to the ovarian surface degenerate earlier than those located deeper in the ovarian stroma.

The liquor of degenerating follicles contains deeply stained chromatin derived from breakdown and dissolved granulosa cells.

There are two distinct forms of follicle degeneration, the regressive and the progressive form.

We have seen here several pictures of the regressive form, which ends with the complete disappearance of the granulosa cells leaving nothing but a cyst without any epithelium.

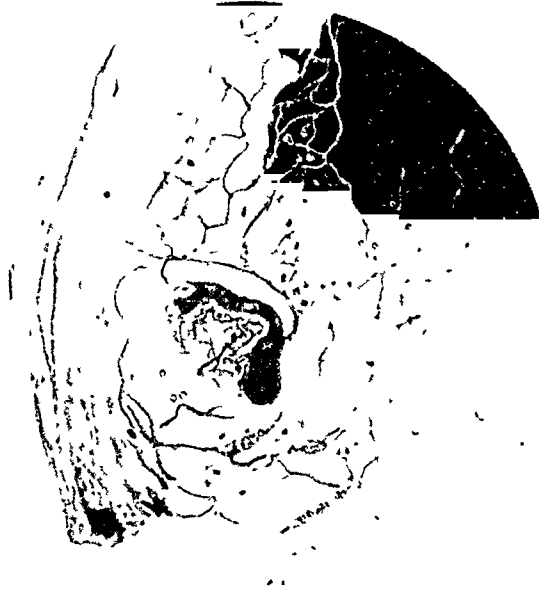


Fig. 12.—Degenerated follicle intravitaly stained. Pseudocorpus luteum. Collapsed ovum deeply stained enclosed in granulosa lutein cells.

The progressive form consists of a transformation of the granulosa cells into lutein cells, which become big by fat accumulation. These cells which fill out the entire follicular cavity do not take any of our stain on account of their fat content. (Fig. 12.) Such a degenerated follicle is not easily distinguished from a true corpus luteum. Only the presence of a degenerated ovum indicates that the follicle did not rupture. The ovum being dead is deeply stained and its shape in its final stages is one of complete collapse, an 'empty shell.

Summary

Intravenous injection of indigo carmine and trypan blue is established as a method for intravital staining of the ovary. Not only the follicle walls, but also the ovum could be visualized. We observed the entire cycle through which most follicles go from the resting stage of the primordial follicle through the stage of the growing Graafian follicle into the various forms of degeneration. We have seen the different,

distinct, and typical ways by which the various forms and elements of ovum and follicle respond to the visible foreign material.

Problems and Conclusions

1. *The Predominant Role of the Ovum.*—Intact ova and granulosa cells do not take the stain. It is a sign of cellular death or degeneration, if the dye appears within the nucleus or the cytoplasm. Intravital staining indicates the beginning degeneration of the ovum at a time when no change of structure is visible. This enabled us to show that the degeneration of any follicle begins in the nucleus of the ovum, progressing further to the ooplasm, and finally to the granulosa cells. In other words, the ovum governs growth and decay of the entire follicle. The findings verify the opinion of Robert Meyer⁹ that the follicle depends upon the ovum in every phase of its development.

2. *The Origin of the Zona Pellucida.*—The zona pellucida of intact ova takes intravital stain. This fact can be used in the discussion concerning the origin of the zona. Early authors (Waldeyer,¹⁰ Pflueger,¹¹ Nagel¹²) claim that the zona is a product of the granulosa cells surrounding the ovum. French authors contend that the zona is produced by the ovum itself. A third group believes that the inner layer of the zona is secreted by the ovum, the outer by the granulosa cells. Our observations show the intimate connection between the zona and the interspaces between the granulosa cells. No connection between the ovum proper and the zona could be visualized. This makes it probable that the zona is deposited from the outside to the ovum, like the calcium deposits of a hen's egg, and not secreted from the inside of the ovum.

3. *The Origin of the Liquor Folliculi.*—The origin of the liquor has been attributed to liquefaction or dissolution of granulosa cells. Some authors believe that the liquor is secreted by the granulosa cells. Our technique of vital staining indicates life or death of any cell. We have not seen one single instance of a degenerating dissolving granulosa cell in a living follicle. We have not observed any secretory activity of the granulosa cell. We have, on the other hand, demonstrated that the liquor depends closely upon the activities of the circulation of blood and lymph. It can, therefore, be concluded that the liquor is a secretory product derived from the blood vessels and the lymphatics, *possibly* modified by the influence of the granulosa cells, but *definitely* not by their liquefaction.

Practical Problems for the Future

A great variety of physiologic and pathologic changes takes place in the ovary during lifetime. In addition, it is exposed to the influence of chemical, physical and electrical factors from the outer world. Medicine, itself, applies methods of treatment in all specialties, which may have some unknown effect upon the ovaries, especially the follicles and ova, in other words, upon the future generation. Two examples to be

named here are the possible effect of radiation and that of an overdosage of estrogens. What amount of damage is done to the germinative cells in these and other instances is of great importance.

Intravital staining as described previously is a method which gives us actual pictures of development and degeneration in the living ovary. It is a test for health, decay and death of any individual ovum and follicle.

It offers itself as a method to study the ovary, also after it has been subjected to any factor which may be pathogenetic. Animals could be treated first by radiation, various drugs, diets, etc., and then their ovaries studied after the dye has been injected intravenously. A wide field of experiments can be visualized in which intravital staining serves as a key which may open the gates to future knowledge and experience.

References

1. Heidenhain, R.: Arch. mikr. Anat. 10: 1, 1874.
2. Krause, R.: Arch. mikr. Anat. 59: 407-416, 1901.
3. Aschoff, L.: Zentralbl. f. allg. Path. u. path. Anat. 23: 625, 1912.
4. Moellendorff, von, W.: Arch. mikro. Anat. 90: 463, 1918.
5. Borell, H.: Beitr. path. Anat. 65: 108, 1919.
6. Goldmann, E.: Beitr. clin. Chir. 64: 192, 1909.
7. Eisler, Bela: Ztschr. Zellenlehre 1: 624, 1924.
8. Strassmann, Erwin: Ztschr. f. Zellforsch. u. mikr. Anat. 21: 545, 1934.
9. Meyer, Robert: Arch. f. Gynäk. 100: 1, 1913.
10. Waldeyer, E.: Eierstock und Ei, Leipzig, 1870, E. F. Flueger.
11. Pflueger, W.: Ueber die Eierstöcke der Säugetiere und des Menschen, Leipzig, 1863.
12. Nagel, W.: Arch. mikr. Anat. 31: 342, 1888.

PAPILLARY LESIONS OF THE CERVIX UTERI IN PREGNANCY

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THE association of proliferative or papillomatous lesions of the cervix with pregnancy presents a problem in etiology and diagnosis which is not generally appreciated. In the literature these have been termed proliferative lesions, papillomas and condylomas.

Cullen¹ states that condylomas may occur during pregnancy and may be mistaken for squamous cell carcinoma.

Norris² in 1913, mentioned that condylomas of the cervix may occur during pregnancy. It was his belief that they were secondary to gonorrheal cervicitis. He recommended histologic examination to exclude carcinoma in such lesions, especially if they presented a cauliflower appearance.

Wharton³ in 1921, considered condylomas of the cervix to be "one of the rarest of gynecological disorders." He reported three cases. Two were gonorrheal in origin, and one was tuberculous.

Hofbauer⁴ in 1933, called attention to proliferative changes in the cervical mucosa and glands during the various stages of pregnancy. These were characterized by hyperplasia of the columnar epithelium, increased mitotic activity, vacuolization of many of the epithelial cells and occasional cell nests in the tissue beneath the mucosa. Squamous metaplasia of the cervical glands and hyperplasia of the epithelium of the squamous portion of the cervix were mentioned. In one of his patients, a small area of proliferation persisted for forty weeks after the termination of pregnancy. Hofbauer believed that the anterior pituitary hormone might be responsible for these growths. He also raised the question of the possibility of such epithelium becoming malignant. In his studies, he found no evidence of epithelial invasion as the cells always rested upon a definite basement membrane. He did not mention any gross changes.

Englander⁵ in 1935, reported seven cases of polyps of the cervix in pregnancy. Though no microscopic examination was done, it was evident from his description that these should be considered in the category of papillary tumors of the cervix occurring during pregnancy. The age of his patients ranged from 19 to 26 years, six were operated upon, and in five excellent results were obtained. Abortion occurred in one, following operation. He described the lesions as both single and multiple growths.

More recently, Mershon⁶ reported two instances of papillomas of the cervix occurring in young women, each aged 22, and in the sixth week of their pregnancies. These were at first diagnosed as squamous cell carcinoma, Grade I, by the pathologist. Additional biopsies and review

of slides by several pathologists resulted in the diagnosis being changed to papilloma in each instance. Both patients were treated with 2,300 milligram hours of radium, which resulted in the prompt disappearance of the tumors. Later biopsies disclosed no evidence of tumor.

DeLee⁷ in his textbook states that he had seen three instances of nodular hypertrophy of the cervix in pregnancy. No further description is given.

We are reporting five cases of clinically evident lesions of the cervix occurring during pregnancy, and one case in which the diagnosis of pregnancy was only presumptive. Our first case has previously been reported by Mershon.



Fig. 1.—Multiple small confluent papillary stalks covered with hyperplastic epithelium. ($\times 100$.)

Case Reports

CASE 1.—F. S., a white married female of 22 years of age, para ii, gravida iv, entered the Los Angeles County Hospital December 15, 1937, with a history of having had cramps and passage of clots on December 10, which was followed by the passage of an embryo. Her last menstrual period had been November 7, 1937. On physical examination, the cervix was observed to have bilateral lacerations and a polypoid circumoral growth. A biopsy was done at the time of dilatation and curettage on December 18, 1937. At this time the uterus was enlarged to one and one-half times normal size. The urine contained an occasional leucocyte and the blood Wassermann was negative. The first diagnosis was carcinoma and the patient was given 2,300 milligram hours of radium between December 27, 1937, and January 3, 1938. Another biopsy was done January 18, which showed no evidence of malignancy. The patient menstruated in February, 1938. When she was last seen in the clinic, on October 9, 1939, there was no tumor present. The cervix was smooth and apparently normal.

Histologic examination of tissue taken on December 18, 1937: A rectangular portion of cervix is composed of cervical glands and thick hyperplastic squamous epithelium. In the latter, there are two types

of changes. The first of these is characterized by a uniformly hyperplastic epithelium with broad, deep, rete cones and long, narrow papillae. (Fig. 5, Case III.) Some papillae appear to have arisen as small buds from the tunica propria and are seen only in the basal portions of the epithelium.

In the second type of change, the epithelium is much thicker. Its architecture in general is that of multiple papillary stalks covered with thick layers of epithelium which fuses indiscriminately with that of other stalks. (Fig. 1.) The papillary stalks do not have a visible tree-like arrangement, but contain multiple small blood vessels and a delicate stroma. The basal epithelium covering the stalks is tall and basophilic. Proceeding outward from the basal layer, the cells mature toward the periphery of each papillary unit much as do cells of the normal squamous epithelium of the cervix. Certain differences, however, can be noted. Throughout the epithelium the nuclei are larger than normal, vary in size to a moderate degree, are hyperchromatic and mitoses are more abundant than normal in the basal portion. Cell borders are fairly distinct and most of the epithelial cells are of the prickle cell variety. In the superficial cells near the surface, a few vacuolated cells are present. Keratinization may be seen in some of the surface cells.

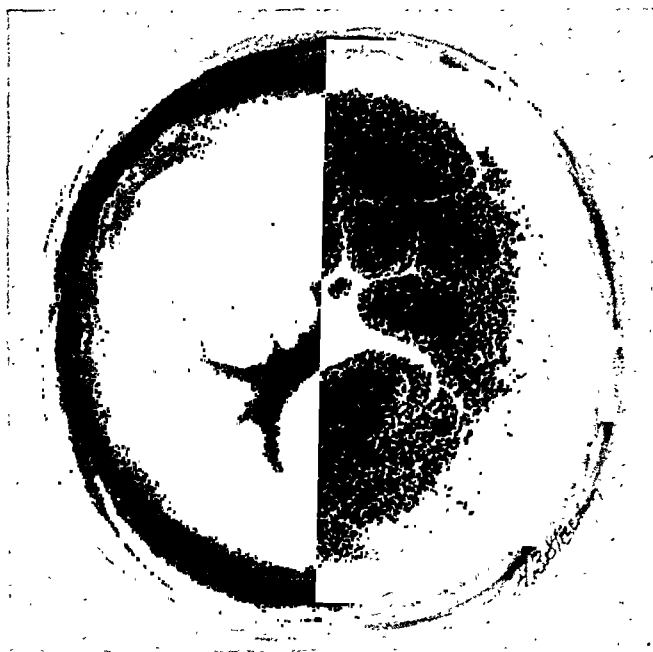


Fig. 2.—Drawing of papillary tumors of the cervix ($1\frac{1}{2}\times$ actual size).

The cervical glands are lined with a single layer of tall, columnar epithelium. Some contain areas of squamous metaplasia. A few of the glands are cystic. Throughout the tissue, there is abundant infiltration with neutrophils. In addition, there are a few areas of round-cell infiltration between the glands.

Small nests of epithelial cells in the connective tissue beneath the basement membrane are occasionally noted. They seem always to rest on a definite basement membrane. These may represent in some instances, complete plugging of the mouths of cervical glands.

CASE 2.—B. A. K. A white married primiparous female of 22 years of age was referred to the hospital for treatment of carcinoma of the



Fig. 3.—Large papillary stalk with multiple side branches. ($\times 30$.)

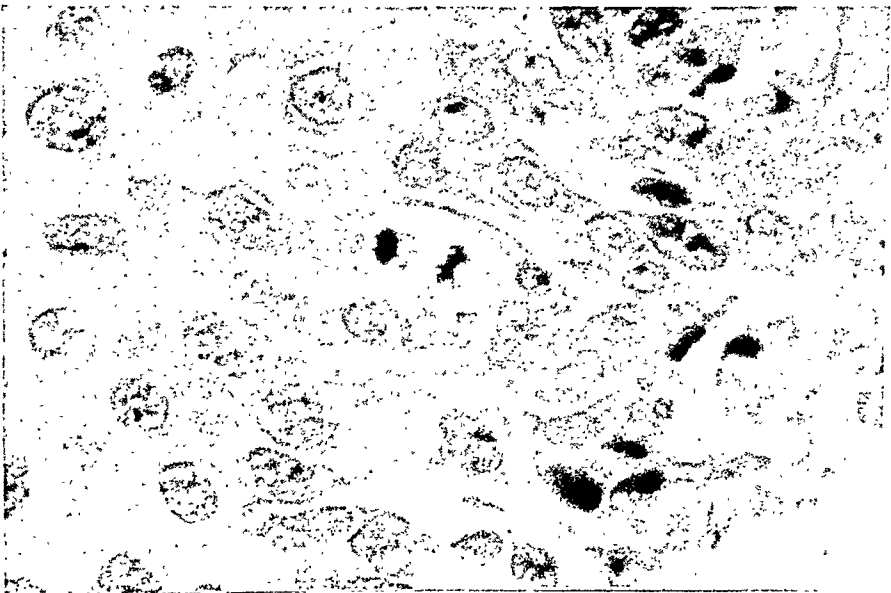


Fig. 4.—Large hyperchromatic nuclei and mitotic figure. ($\times 450$.)

cervix, Grade III. She entered February 7, 1940, nine days post partum, following delivery of a full-term baby at another hospital. Delivery had been aided by insertion of a bag to control hemorrhage. Patient stated she had had some white discharge since onset of menstruation at the age of thirteen. On examination, large papillary tumors of the cervix were noted. (Fig. 2.) The blood Wassermann was negative. On February 19, the cervix was given 800 milligrams radium (filtered through 1 mm. platinum). The appearance of the cervix began to improve promptly after treatment, but it was not entirely free of change until May 7, 1940. Beginning March 16, 1940, menstrual periods have been regular.

Histologic examination of tissue removed on February 19: This illustrates a third type of change in epithelial overgrowth. There are multiple, large, discrete, papillary growths of various sizes (up to 5 mm. in diameter). They have a central connective tissue stalk, in which there are many blood vessels and an occasional cervical gland. (Fig. 3.) From the large central stalk, branching papillary processes extend into thick squamous epithelium, and finally, near the surface, the smaller papillary stalks end in an arrangement similar to the second type described above. In the superficial portions of the tumors vacuolated cells are common. Mitoses are numerous. (Fig. 4.)



Fig. 5.—Broad deep rete cones and long narrow papillae. ($\times 25$.)

CASE 3.—J. E. C. A white married primiparous female of 18 entered the hospital August 16, 1940, in labor and at term. A low forceps delivery was done after six hours of labor. At time of delivery, a gray-white ulcerated lesion of the squamous portion of the cervix was noted. It extended throughout most of the circumference of the cervix near the external os. A biopsy was done at this time.

The blood Wassermann was negative. The urine was without change. The patient returned for examination four weeks post partum, on September 12, 1940, at which time only a thin, white scar could be seen on the cervix. Further periodic examinations were done and a cauteriza-

tion of the affected area on the cervix was performed on October 31, 1940. Cervix was pronounced completely healed on June 19, 1941.

Histologic examination of tissue taken at time of delivery: The section contains both cervical glands and thick masses of hyperplastic squamous epithelium. The changes differ little from those seen in Case 1. Acute inflammatory changes are rife. The broad, deep rete cones and long papillae are especially noticeable. (Fig. 5.) There is some squamous metaplasia of the cervical glands. (Fig. 6.)



Fig. 6.—Squamous metaplasia of cervical glands. ($\times 150$.)

CASE 4.—R. L. A white married primiparous female of 22 years of age, first entered the hospital on August 9, 1941, because of sudden pain in left upper quadrant, localizing in the right lower quadrant. There was moderate tenderness and guarding of the abdomen. The patient was operated on and several necrotic hydatids of Morgagni were removed. An early intrauterine pregnancy was observed. Recovery was uneventful. The patient next entered the hospital on October 7, 1941, for the removal of a condylomatous growth on the cervix, diagnosed in the outpatient department. She had complained of excessive vaginal discharge. The blood Wassermann and Kahn tests were negative. Cervical smears and complement fixation tests were both negative for gonorrhea. On examination, three large cauliflower growths, 2 to 3 cm. in length were seen on the cervix. These were removed by dividing them at their base and cauterizing the bleeding points. The patient delivered a full-term, 7-pound baby on April 15, 1942, at which time no mention was made of the cervix.

Histologic examination of tissue taken on October 7, 1941: There are large masses of hyperplastic epithelium in which a few cervical glands are present. Much of the growth has taken the form of large discrete papillary stalks, similar to that seen in Case 2. Areas of early keratinization are present; some of these form small "pearls." Vacuolization of the epithelial cells is common (Fig. 7).

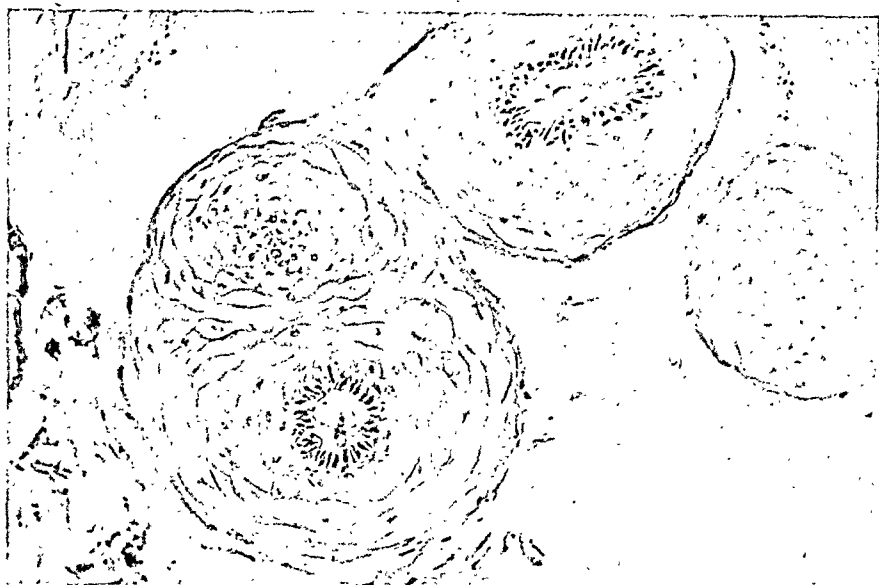


Fig. 7.—Vacuolization of epithelial cells covering papillary stalks. ($\times 100$.)

CASE 5.—M. M. A 17-year-old white married female came to the hospital on September 22, 1941, complaining of painful breasts and vaginal bleeding of four days' duration. This has followed a period of amenorrhea, which began following a menstrual period on July 1, 1941. On examination, the cervix was soft and the corpus was slightly enlarged. Blood Wassermann and Kahn tests were negative. The urine contained many pus cells. Dilatation and curettage was done on September 29, 1941. This showed no evidence of pregnancy. Her second entry to the hospital was on December 4, 1941. Again, she was considered a possible pregnancy because of a missed period in October. Cramps and vaginal bleeding had been present for twelve hours. A biopsy was taken of the cervix because of a small papilloma. Histologically, this is similar in all respects to Case 1. Mitoses were particularly abundant (Fig. 8). The patient returned several times to the clinic and, when last seen on April 20, 1943, the lesions had disappeared except for a small cervical erosion. She still complained of a vaginal discharge. Repeated cervical smears were negative for gonococcus.

This is a case of presumptive pregnancy only, but it is included because of the resemblance of the tumor growth to the others, and it presented much the same clinical problem.

CASE 6.—L. C. A. A primiparous Mexican female of 17 years of age, entered the hospital on February 12, 1942, at term and in labor. She delivered spontaneously a 7-pound, 2-ounce male infant. When a repair of cervical lacerations was done following delivery, a small pearl-white area of thickening was seen on the cervix. A portion was removed for histologic examination. So far the patient has not returned to the obstetric clinic.

Histologic examination: There is a small nubbin of epithelium projecting above the cervical mucosa. (Fig. 9.) Its architecture is that of the second-type lesions, i.e., thickening of the squamous epithelium with multiple small, papillary stalks.

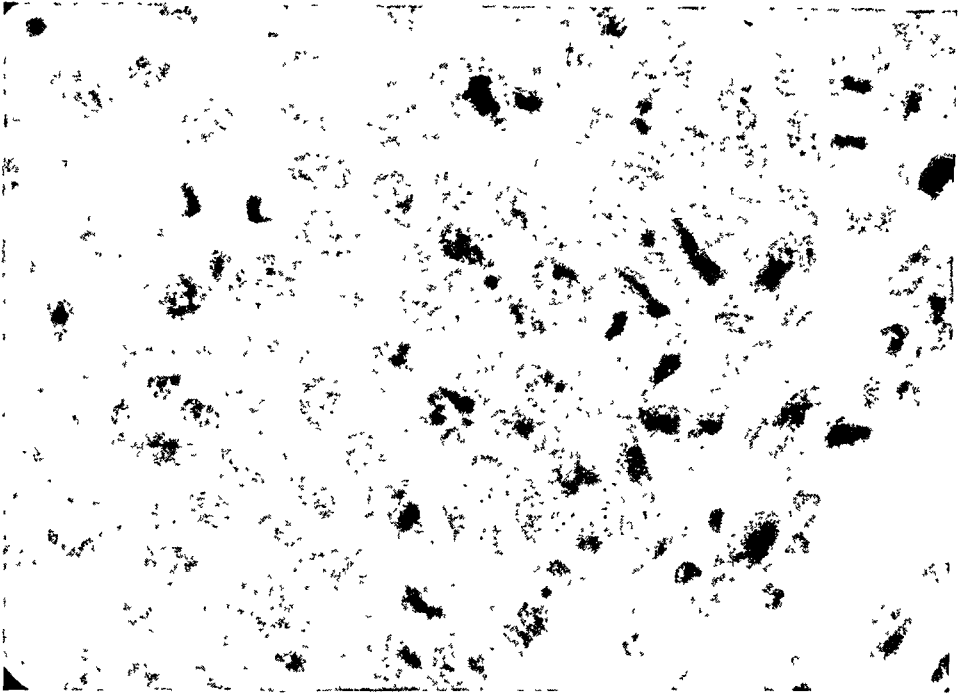


Fig. 8.—Many mitoses, hyperchromatic nuclei and variation in size of nuclei are suggestive of cancer. ($\times 450$.)



Fig. 9.—Small solitary papillomatous lesion. ($\times 20$.)

Comment

The changes seen in the cervixes studied may be conveniently divided into three groups. Type 1 and 2 lesions are practically always seen together, although in Case 5 (M.M.), one specimen shows only Type 1 change, but as a rule this type is noted only at the margins of the lesions.

The histologic changes characteristic of Type 1 are simple hyperplasia of the squamous epithelium with the formation of large, rete cones between which there are long, narrow papillae. Epithelial mitoses are more frequent than normal.

The macroscopic appearance of a cervix with Type 2 change is that of irregular nodular areas of gray-white or pearly thickening. Although the clinicians interpreted these as being on the portio vaginalis, cervical glands were always present which indicated that the tumor originated in the proximity of the external os. Microscopically, these differ from Type 1 in that the masses of epithelium are two to three times as thick, and the cells are arranged around papillary stalks.

In Type 3 change, there were gross papillary growths, or condylomas, some of which were 2 to 3 cm. in length. They arose in the same areas, near or at the external os. They had large central stalks, with a multitude of papillary side branches covered with thick squamous epithelium similar to that seen in other types.

Vacuolization of the cytoplasm of the cells, especially in the older, more superficial portions of the tumor, and evidence of acute inflammation both in the papillomatous growth and the adjacent cervical tissue, were present in all of the types of change observed. In addition, squamous metaplasia of the glands of the endocervix and proliferative changes in the columnar epithelium of the cervical glands, as described by Hofbauer, were seen in three of the tumors.

One of the noticeable histologic features of these tumor-like lesions is the rather large number of mitotic figures among the epithelial cells. This fact seems important as it suggests the possibility of carcinoma and somewhat complicates the pathologist's problem in reaching a diagnostic decision. In an effort to determine the significance of the fairly numerous mitotic figures, careful estimates of their numbers were made in the sections from the cases here reported. These counts were compared with the findings in similar biopsy sections from two other groups of patients, as indicated in Table I. The second group comprised young women who were pregnant or had had recent abortions, but who were without evident cervical lesions. The third group were young women who had not had recent pregnancies, and whose cervical tissues were apparently normal.

The obvious inferences to be derived from the data in Table I seem to be that the rate of mitosis in the stratified squamous epithelium of the normal cervix tends to be less than that of the pregnant uterus, while in the papillary lesions of the cervix in pregnancy the rate is still higher.

The significance of these data may be lessened by the small number of cases observed and by the wide variations in the mitotic counts in each group; however, they are presented for what they are worth.

One of the factors possibly concerned in the variations in the counts within the groups is that of natural rhythmicity of mitosis in animal

TABLE I. MITOSIS COEFFICIENT*

1. Papillary lesions of pregnancy 6 cases—ages 17 to 23 years	0.8 to 4.8	Average 2.12
2. Pregnancy or abortion 8 cases—ages 16 to 36 years	0.0 to 3.2	Average 0.93
3. Nonpregnant. Normal cervix 6 cases—ages 23-43 years	0.0 to 0.32	Average 0.14

*Mitosis coefficient—number of mitotic figures per 1,000 tissue cells. See Broders and Dublin: Rhythmicity of Mitosis in the Epidermis of Human Beings, Proc. Mayo Clinic 14: 423, 1939.

tissues. Recent studies which have been reported, are based upon observations of tissues of young animals, the foreskins of human infants one week old, and upon certain malignant tumors. These observations are, on the whole, of limited volume, but lead to the following tentative conclusions:

1. Normally growing tissues exhibit a definite diurnal rhythm of mitosis, the maximum intensity averaging from 2 to 4 times the minimum.
2. The rhythm differs as to time and intensity in different kinds of animals, and in different organs in the same animals.
3. Malignant tumors fail to exhibit any recognizable rhythm. In other words, the mitotic activity is independent of the rhythm of normal body tissues; that is, cancerous tissue growth is uniformly constant, without diurnal periodicity.

It may well be that the variations shown in our groups were in part related to natural diurnal periodicities. Other possible influences might be assumed such as a rhythmicity associated with the menstrual cycle. So far as we are aware, no observations intended to determine such variations have been reported.

It must be recognized that chronic inflammatory lesions of non-pregnant cervixes present certain microscopic features similar to those which have been described in these papillary lesions of pregnancy. But, it is our observation that in such inflammatory lesions we do not find (1) an equal degree of mitotic activity, (2) hyperchromatism and inequality of nuclei of similar grade, (3) frank papillomatous changes of sufficient size and complexity to be recognized as condylomatous.

Condylomas of the cervix occurring in the absence of pregnancy are indeed rare. At the Los Angeles County Hospital our records are not complete, but in our experience, we have seen it only once.

It is evident that these growths are not malignant in that they are not invasive. The question arises as to whether they may be a pre-malignant lesion and some time after pregnancy may become invasive. However, carcinomas of the cervix reported during pregnancy occur for the most part in an older age group, i.e., 30 to 40. Nowhere in the literature were we able to find that such benign papillary lesions had been described as antecedent to carcinoma. The possibility remains, however, that they may become malignant.

The etiology of these papillary growths is not known. Hofbauer believed that the anterior pituitary hormone may be responsible for proliferative changes in the cervical glands. Certain experimental work, however, indicates the importance of estrogen as a cause of proliferative changes in the vagina and cervix. Overholser and Allen⁸ produced atypical growths in the epithelium of the cervix of the monkey by the use of prolonged injections of ovarian hormone combined with trauma. These were not autonomous growths as they disappeared with cessation of hormone administration. V. Suntzeff⁹ et al. produced carcinoma-like growths in the vagina and cervix of mice with the injection of large doses of estrogen. In experiments with hybrid mice, Allen and Gardner¹⁰ produced squamous cell cancer of the cervix by the long-continued use of estrogen (16.6 mg. to 50 mg. of estradiol benzoate per week) in animals which survived the treatment for more than one year. Crossen and Loeb¹¹ produced similar lesions in mice which had passed the reproductive period by the same means.

Another likely etiological factor is infection. Because of vaginal discharge, two of our patients were suspected of having gonorrhea but this was not proved by smear or complement fixation test. Nonspecific chronic cervicitis, with discharge of irritating secretions might provoke such a growth. The microscopic evidence of diffuse acute inflammation of both the hyperplastic tissue and the underlying cervix gives credence to this theory.

The ages of the patients, 22, 22, 18, 22, 17 and 17, with an average of 19.6 years, is probably significant. The ages of these patients are similar to those reported by Englander and Mershon.

In summation, one might postulate that in young pregnant women in whom perhaps the tissues of the body have not yet completely finished their growth cycle, the action of the hormones associated with pregnancy, particularly estrogenic hormone, combined with infection of the cervix may give rise to papillary overgrowth of the squamous epithelium at or near the external os.

That these lesions should be recognized as benign and not treated as cancer is a lesson to be remembered by clinician and pathologist alike. This cannot be overemphasized. The pathologist must give careful attention to the clinical history as well as to the histologic criteria that differentiates these lesions from carcinoma. Only in this way can mistakes be avoided. In the last analysis, the following triad forms the basis of correct diagnosis and sound judgment in the treatment of these lesions: (a) Youth, (b) pregnancy, (c) lack of invasion of cervical tissue by the epithelial growths.

Summary and Conclusions

1. Five instances of proliferative or papillary lesions of the cervix uteri associated with pregnancy are reported. One case of presumptive pregnancy is included.

2. The ages of the patients varied from 17 to 22 years. The average was 19.6 years.

3. The lesions were seen at various stages of pregnancy ranging from the second month to the time of delivery.

4. The proliferative growths were single or multiple, varied in size from small pearly gray-white areas to papillomas raised 2 to 3 cm. above the surface and were always located at or near the external cervical os. Usually they were described as being circumoral.

5. Microscopically, they were characterized by various grades of proliferative change in the squamous epithelium, i.e., (a) simple thickening of the epithelium; (b) greatly thickened irregular epithelial units indiscriminately fused together with confluent tiny papillary stalks; (c) large papillomatous growths.

6. Cellular changes such as irregularity in size of nuclei hyperchromatism, unusual mitotic activity and vacuolization of the cytoplasm may tend to confuse the diagnosis with carcinoma. True invasion, however, does not occur.

7. The etiology is not clear. Age, hormones and infection may all be responsible.

8. The treatment is conservative. Large, discrete tumors can be removed surgically. Radiation therapy is of value in treating extensive multiple lesions.

References

1. Cullen, T. S.: *Cancer of the Uterus*, Philadelphia, 1909, W. B. Saunders Co., p. 191.
2. Norris, C. C.: *Gonorrhea in Women*, Philadelphia, 1913, W. B. Saunders Co., p. 231.
3. Wharton, Lawrence R.: Rare Tumors of the Cervix and the Uterus of Inflammatory Origin—Condyloma and Granuloma, *Surg., Gynec. & Obst.* 33: 145, 1921.
4. Hofbauer, J.: Epithelial Proliferation in the Cervix Uteri During Pregnancy, and Its Clinical Implications, *AM. J. OBST. & GYNEC.* 25: 779, 1933.
5. Englander, B.: Polypus of the Cervix of the Uterus and Pregnancy, *Polska Gaz. Lek.* 14: 183-184, 1935.
6. Mershon, Henry F.: Pregnancy and Malignant ? Lesions, *Radiol. Rev. & Mississippi Valley M. J.* 60: 132, 1938.
7. DeLee, Joseph B.: *The Principles and Practice of Obstetrics*, Philadelphia, 1938, W. B. Saunders Co., p. 598.
8. Overholser, M. D., and Allen, E.: Atypical Growth Induced in Cervical Epithelium of Monkey by Prolonged Injections of Ovarian Hormone Combined with Chronic Trauma, *Surg., Gynec. & Obst.* 60: 129-136, 1935.
9. Suntzeff, V., Burus, E. L., Moskop, Marian, and Loeb, Leo.: On the Proliferative Changes Taking Place in the Epithelium of Vagina and Cervix of Mice With Advancing Age and Under the Influence of Experimentally Administered Estrogenic Hormones, *Am. J. Cancer* 32: 256, 1938.
10. Allen, E., and Gardner, W. U.: Cancer of the Cervix of the Uterus in Hybrid Mice Following Long-Continued Administration of Estrogen, *J. Cancer Research* 1: 359-366, 1941.
11. Crossen, R. J., and Loeb, Leo.: Effect of Long-Continued Administration of an Estrogen on the Sex Organs of Mice Which Have Passed the Reproductive Period, *Arch. Path.* 37: 202, 1944.

MANUAL REMOVAL OF THE PLACENTA

A Policy of Treatment

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RETENTION of the placenta following delivery has always been considered a major complication in obstetrics. The high maternal mortality associated with this complication justifies such an attitude.^{1,2} Death usually is caused by sepsis or by hemorrhage with its accompanying shock. In recent years, with the advent of effective therapeutic agents for combating infection and with the availability of large quantities of blood for immediate transfusions, the mortality rate associated with manual removal of the retained placenta has been steadily reduced.

Although in obstetric literature, considerable attention has been devoted to manual removal of placenta, we believe that certain aspects of this problem have not been emphasized sufficiently. The need of a general policy for routine treatment of this condition is desirable. We believe that the treatment is dependent upon the solution to two fundamental questions, namely:

1. If spontaneous expulsion of the placenta does not occur, how much time should elapse before a manual removal is indicated?

When spontaneous expulsion of the placenta has failed, one should be able to establish an optimal time for attempting manual removal in order to prevent serious effects from hemorrhage. Furthermore, one should expect a lower incidence of sepsis when the blood loss is kept at a minimum. This is in accordance with the practice of good obstetrics.

2. Is there evidence that placental retention is associated either with abnormal uterine function or with faulty implantation of the placenta?

The failure of spontaneous expulsion of the placenta usually is attributed to (1) "failure of separation," (2) separation with retention because of "hour-glass" constriction of the lower uterine segment, (3) the so-called "adherent placenta."

With the use of the active principle of ergot (ergonovine), given intravenously (when the infant's anterior shoulder is born), the physiology of normal placental separation must be revised. Apparently, separation occurs because of the immediate marked decrease in the size of the placental site. Certainly, there is no evidence that separation occurs by the classical formation of the retroplacental hematoma, because, in most instances, the separation is so rapid and complete that such a hematoma usually is not found. Although "failure of separation" of the placenta per se can occur, the incidence should be much lower with the use of intravenous ergotrate, because placental

separation is markedly enhanced by this drug. It may be argued that the routine use of ergotrate results in an increased incidence of "hour-glass" constriction of the lower uterine segment. This may be true. However, failure of expulsion of the placenta because of this "hour-glass" constriction is compensated by the increase in the number of placentas which separate. Hence, the necessity for manual removal should not be increased.

If, with the use of this oxytocic, "failure of separation" does not occur, one may assume that the failure of expulsion is a result of the "adherent placenta" caused by placenta accreta, rather than by poor uterine function. Placenta accreta is the coherence of the placenta to the myometrium, resulting from the absence of the decidual basalis, particularly of the stratum spongiosum. Such accretion may be produced by either direct contiguity to or invasion of the myometrium by the chorionic villi, or by myometrial incursion into the placenta septa. These changes may involve all or portions of the maternal surface of the placenta. Consequently, this involvement may be classified as complete, partial or focal. The complete type implicates all of the cotyledons of the placenta, the partial, one or several, and the focal, a portion of only one cotyledon.

Incidence.—Manual removal of a retained placenta following the delivery of a viable infant was performed 217 times at the Boston Lying-in Hospital from 1920 to 1943, inclusive. During that period, 45,602 patients were delivered of viable infants. Manual removal of the placenta was performed once in every 210 deliveries or 0.47 per cent. Twenty-nine (13.1 per cent) of the 217 patients were delivered in the home.

TABLE I. INDICATIONS FOR MANUAL REMOVAL .

INDICATIONS	TOTAL CASES	PER CENT
Hemorrhage	116	53.4
Retention	101	46.6

Indication for Manual Removal.—The indications demonstrated in Table I have been divided into two groups, namely, hemorrhage per se, and retention with hemorrhage. During a period from 1920 to 1930, there were only forty cases of manual removal. A large percentage of these cases was occasioned by hemorrhage following delivery by accouchement forcé. During recent years, the chief indication has been retention.

Duration of Pregnancy.—The duration of pregnancy could be determined accurately in most cases. Approximately one-fourth of the cases (22.1 per cent) of manual removal occurred in patients who delivered prematurely, as shown in Table II. Three-fourths of the patients delivered at term. This study does not substantiate the general opinion that a large percentage of retained placentas is associated with premature labor.² The size of the infant at term appears to be an unimportant

TABLE II. DURATION OF PREGNANCY

PREGNANCY BY WEEKS	TOTAL CASES	PER CENT
28 to 34 weeks	17	7.8
34 to 38 weeks	31	14.3
38 to 42 weeks	163	75.2
Over 42 weeks	6	2.7

factor. The incidence of postmaturity is only 2.7 per cent, and, therefore, does not constitute a significant factor.

Duration of Labor.—The general opinion that prolonged labor increases the morbidity rate following manual removal is not confirmed by analysis of our series, as demonstrated in Table III. Schwartz and Richards³ reported a morbidity rate of 71.4 per cent for patients who were in labor over thirty hours, and seven of them were febrile in the puerperium. The morbidity rate in this group was 30.4 per cent, which is only slightly higher than that of the large group of patients who were delivered within thirty hours (26.6 per cent) after the onset of labor. However, 10.6 per cent of the patients were in labor over thirty hours. This confirms the general impression that prolonged labor is a factor in placental retention.

TABLE III. MORBIDITY—RELATION TO LENGTH OF LABOR

HOURS OF LABOR	TOTAL CASES	MORBIDITY	
		NUMBER OF CASES	PER CENT
Under 10	101 (46.5%)	26	25.7
10 to 20	73 (33.7%)	25	34.2
20 to 30	20 (9.2%)	4	20.0
30 and over	23 (10.6%)	7	30.4

TABLE IV. MORBIDITY—RELATION TO TYPE OF DELIVERY

	NORMAL DELIVERIES		OPERATIVE DELIVERIES		MORBIDITY			
					NORMAL DELIVERIES		OPERATIVE DELIVERIES	
	TOTAL CASES	PER CENT	TOTAL CASES	PER CENT	NUMBER CASES	PER CENT	NUMBER CASES	PER CENT
Primiparas (42.4%)	30	32.6	62	67.4	9	30.0	17	27.4
Multiparas (57.6%)	88	70.4	37	29.6	24	27.2	12	32.4

Type of Delivery.—Delivery effected either by normal or by operative procedures apparently does not alter the morbidity rate, as exhibited in Table IV. There is a slightly increased morbidity rate following manual removal of placentas in multiparas who were delivered by operative procedures.

Maternal Morbidity.—There were sixty-two morbid patients in this series, following manual removal, as demonstrated in Table V. Excluding two patients who died within twenty-four hours, the morbidity rate for 215 cases is 28.8 per cent. Excluding the ten patients who were febrile after subtotal hysterectomies, the corrected rate is 24.1 per cent. In this group of ten cases, placenta accreta was found in nine instances.

The remaining patient underwent a hysterectomy because the uterus was ruptured during the manual removal. This is the only instance of ruptured uterus in this series, but its very possibility definitely emphasizes the need of extreme gentleness on the part of the operator.

TABLE V. MATERNAL MORBIDITY AND MORTALITY RATES

TOTAL CASES	MORBIDITY		CORRECTED MORBIDITY		MATERNAL MORTALITY		
	TOTAL CASES	PER CENT	TOTAL CASES	PER CENT	NUMBER CASES	PER CENT	CORRECTED
217	62	28.8	52*	24.1	4	1.8	1.3%†

*Excluding 10 patients who were febrile after hysterectomy.

†Excluding a patient who died from pneumococcic meningitis.

TABLE VI. MORBIDITY—RELATION TO BLOOD LOSS

AMOUNT IN C.C.	TOTAL CASES	MORBIDITY	
		NUMBER OF CASES	PER CENT
Under 500	129	27	20.9
500 to 1,000	66	24	36.3
Over 1,000	22	11	50.0

TABLE VII. MORBIDITY—TIME OF PLACENTAL RETENTION

HOURS RETAINED	TOTAL CASES	MORBIDITY		AVERAGE BLOOD LOSS C.C.
		NUMBER CASES	PER CENT	
Under 1 hour	77 (35.5%)	18	23.3	339
1 to 2	63 (29.0%)	13	20.6	406
2 to 3	27 (12.5%)	10	37.0	598
Over 3 hours	50 (23.0%)	21	42.0	544
Totals	217	62	28.8*	471

*Excluding two patients who succumbed within twenty-four hours.

The important factors which appear to influence the morbidity rate are presented in Tables VI and VII. Table VI emphasizes the fact that the morbidity rate is markedly increased in proportion to the degree of blood loss. Table VII reveals an increase in the morbidity rate in relation to the elapsed time from delivery until the time of manual removal. The correlation between the blood loss and the elapsed time, together with their relationship to the morbidity rate, is impressive.

Mortality.—Four patients out of the 217 in this series died following manual removal of the placenta. The uncorrected maternal death rate is 1.8 per cent. Excluding the patient who died on the twelfth postpartum day from pneumococcic meningitis, the corrected mortality rate is 1.3 per cent.

The case histories of the four deaths are summarized as follows:

CASE 1.—(1928.) Mrs. B. is a 23-year-old para iii. She was three and one-half weeks overdue by dates. After five hours of labor, the patient was delivered normally of an infant weighing 9 pounds, 6¼ ounces. The placenta failed to separate within the allotted time, profuse bleeding

followed, and the patient went into shock. Two blood transfusions were given. One hour and forty minutes after delivery, a manual removal was attempted. Part of the placenta was removed in pieces. During this procedure, the uterus was inverted. The remainder of the placenta could not be removed; therefore, the uterus was replaced and a rapid supravaginal hysterectomy was done, without anesthesia. The patient succumbed to shock and hemorrhage five and one-half hours after delivery. Permission for autopsy could not be obtained. Microscopic examination of the placenta showed a partial placenta accreta.

CASE 2.—(1934.) Mrs. McK. is a 28-year-old, unregistered para vi. The patient had a precipitate delivery at home, which was followed by profuse vaginal bleeding because of retained secundines. She was admitted to the hospital one and one-half hours later in profound shock. Two blood transfusions were given, and a manual removal of the placenta was done. The patient was afebrile until the eleventh postpartum day. She then experienced a chill and the temperature rose to 104 degrees. She had a convulsion. The neck was found to be stiff. A lumbar puncture revealed the spinal fluid to be turbid with a cell count of 2,500. Stained smears showed gram-positive diplococci. In spite of serum therapy, the patient succumbed on the twelfth postpartum day. Autopsy findings showed a pneumococcal meningitis.

CASE 3.—(1936.) Mrs. R. is a 22-year-old primipara at term. After forty-seven and one-half hours of desultory labor, the patient was delivered of a 9 pounds, 1 ounce infant by low forceps. In spite of the use of pituitrin and several attempts at Credé and Gabeston-Monjon maneuver, the placenta could not be delivered. Therefore, three hours after delivery, a manual removal of the placenta was done. The atonic uterus required gauze packing. A blood transfusion was given. The total blood loss was estimated to be 500 cubic centimeters. The patient became febrile, with a temperature of 106 degrees by the third postpartum day. An intrauterine culture grew anaerobic streptococci. Prontosil was given without any therapeutic response. During the course of the next twenty-three days, the patient continued to be febrile. Seven more blood transfusions were given. An x-ray of the chest showed evidence of pulmonary infarction. On the thirty-sixth postpartum day, the patient succumbed to bronchopneumonia. Permission for autopsy could not be obtained.

CASE 4.—(1939.) Mrs. McC. is a 33-year-old para iv, who was delivered of twins at home in the twenty-ninth week. The patient was transferred to the hospital several hours later because the placenta failed to separate. Seven and one-half hours after delivery, manual removal of the placenta was attempted. Part of the placenta was removed in pieces. The uterus was packed because of profuse hemorrhage. A supravaginal hysterectomy was done. In spite of six blood transfusions (3,600 c.c.), the patient succumbed within twenty-four hours. An autopsy was performed. Microscopic examination of the placenta showed multiple areas of focal accreta.

It is obvious that two of these patients succumbed to shock and hemorrhage because of forceful piecemeal removal of retained placentas which proved to be placenta accretas. The other two patients died from infection. It is difficult to believe that manual removal was the fatal factor

in causing the death of the patient who succumbed to pneumococcal meningitis. The patient who died of bronchopneumonia evidently had infected pulmonary emboli which probably originated from a thrombophlebitis of the pelvic veins. Undoubtedly, the infection was introduced at the time of the manual removal.

TABLE VIII. UTERINE TAMPONADE AFTER MANUAL REMOVAL

TOTAL CASES	AVERAGE BLOOD LOSS C.C.	TOTAL NUMBER OF TRANSFUSIONS	AVERAGE TRANSFUSION PER PATIENT	MORBIDITY	
				NUMBER OF CASES	PER CENT
18 (8.1%)	933	47	2.9 (1,467 c.c.)	10	55.5

Uterine Tamponade.—Eighteen patients (8.2 per cent) in this series had uterine tamponade. The morbidity rate is 55.5 per cent. Uterine atony was the indication for packing in twelve of these patients following successful manual removal of the placenta. The high morbidity was undoubtedly influenced by the severe blood loss which made uterine packing imperative. The remaining six patients had placenta accretas, four of whom underwent supravaginal hysterectomies. Excluding these four cases, the morbidity rate is 42.8 per cent. Sulfanilamide gauze packs were used in five patients. Two of the patients became febrile, establishing a morbidity rate of 40.0 per cent. This small series of sulfanilamide gauze packs does not merit a definite conclusion, but it is believed that the use of such packs will lower the morbidity rate. Uterine tamponade, if necessary, should be undertaken as a separate procedure with utmost regard for asepsis.

Placenta Accreta.—It is not the purpose of this paper to discuss the clinical entity of placenta accreta in detail. This obstetric complication has been thoroughly studied in a report by Irving and Hertig.⁴ Those authors report an incidence of one case of placenta accreta in every 1,956 deliveries.

TABLE IX. RETAINED PLACENTAS DUE TO PLACENTA ACCRETA

TOTAL CASES	PARITY		AVER- AGE BLOOD LOSS C.C.	TYPE OF ACCRETA			TREATMENT		OUTCOME OF PATIENT	
	PRIMIP- ARAS	MULTIP- ARAS		FO- CAL	PAR- TIAL	COM- PLETE	MAN- UAL RE- MOVAL	HYS- TEREC- TOMY	LIVED	DIED
24 (11.0%)	5 (21.0%)	19 (79.0%)	1,041	2	20	2	7	17	22	2 (8.3%)

In this series of 217 cases where manual removal of the placenta was attempted, some degree of placenta accreta was encountered twenty-four times. This represents an incidence of 11.0 per cent (Table IX) or once in every 1,900 deliveries. All of these cases of placenta accreta were

verified by careful microscopic study.⁵ We would emphasize the increased degree of blood loss, morbidity and maternal mortality rates occurring in this group of patients.

Oxytocic Drugs Following Delivery.—The use of oxytocic drugs following the delivery of the infant did not appear to be a significant etiologic factor in retention of the placenta. Approximately one-half of the cases did not receive pituitrin or ergotrate after delivery of the infant. The incidence of retained placentas, in relation to total deliveries, was greater in the patients who were delivered at home, where oxytocic drugs were not used until after the expulsion of the placenta.

Infant Deaths.—Two hundred and twenty-three viable infants were delivered from the 217 patients in this series. This figure includes six sets of twins, or an incidence of one in every thirty-six patients (2.7 per cent). Six patients had hydramnios and were delivered of fetal monsters. These two groups (twins and hydramnios) appear to be somewhat significant, as they comprise 5.5 per cent of the cases. There were ten macerated stillborn infants, establishing an incidence of 4.9 per cent. The gross fetal mortality rate for the 217 cases is 11.2 per cent. Excluding the ten macerated infants, the rate is 7.0 per cent. Excluding three fetal monsters, the corrected fetal death rate is 5.7 per cent. We believe that macerated infants, twins, and hydramnios are etiologic factors worthy of consideration.

Miscellaneous.—The history of manual removal of the placenta in preceding pregnancies was not frequent. In this series, it was encountered only four times in three patients. There were surprisingly few patients who had previous abortions and curettements. One patient had been delivered in the preceding pregnancy by a classical cesarean section. Following a pelvic delivery, the retained placenta was found to be accreted in the region of the old section scar. Two patients had multiple uterine fibroids. Eleven patients had pregnancy toxemias.

Placental abnormalities, such as circumvallate, bipartite, and succenturiate lobes, were encountered in 5.0 per cent of the cases. Two patients had previous placenta previas, and two had previous toxic separation of normally implanted placentas.

Transfusions.—In this series of 217 patients, sixty-nine (31.7 per cent) were transfused. To these sixty-nine patients, 132 transfusions were given, an average of 1.9 transfusions per patient. Ninety-one transfusions, or 68.9 per cent of all the transfusions, were given to thirty-four patients who had either placenta accreta or uterine tamponade, making an average of 2.7 transfusions per patient for this group. It has been the policy of this clinic for the past fifteen years to have available donors conveniently at hand whenever a manual removal is performed.

Recently, a modified blood bank has been established. Group O Rh-negative and Group O Rh-positive blood are stored in adequate quanti-

ties. The blood is drawn into a flask containing 500 c.c. of a special preservative which enables us to store the blood for at least thirty days. The a and b factors of the serum are treated by Witebsky's inactivating substance, which obviates the necessity of cross-matching.

Routine blood grouping and Rh factor determination are done on all of our patients at the first prenatal visit. If the need arises, Rh-positive or Rh-negative blood can be given immediately, according to the Rh status of the patient. Emergency patients who require transfusions are always given Rh-negative blood until the Rh factor has been determined.

Discussion and Treatment

It appears evident that the problems associated with the retained placenta are influenced by hemorrhage, sepsis, and faulty implantation of the placenta.

A morbidity rate of 20 to 25 per cent in the least complicated cases must, at least for the present, be accepted.* This rate is markedly increased if the blood loss exceeds 500 c.c. per patient. In order to prevent such blood loss, it is imperative that the placenta should not be allowed to remain in the uterus longer than one to two hours. Certainly, nothing is gained by permitting the placenta to be retained for a longer period of time.

We believe that the term "failure of separation" should be retained. In these cases, a complete line of cleavage can readily be established. Failure of separation in this instance, obviously, results from poor uterine function. Since establishing the routine use of intravenous ergotrate, administered when the infant's anterior shoulder is born, we have not observed any increase in the number of retained placentas. If retention does occur, the causation is more likely a result of "hour-glass" constriction than of "failure of separation." Furthermore, even if expulsion does not occur after the use of this drug, we have been impressed by the small blood loss associated with placental retention.

Faulty implantation of the placenta (placenta accreta), popularly termed "adherent placenta," should be regarded as an important, not infrequent, and very serious cause for retention of the placenta. We are aware of the fact that the incidence of placenta accreta is exceptionally high in this series. We are not cognizant of such an incidence in any previously reported series of manual removal. A diagnosis of placenta accreta should be made, we believe, when a clear line of cleavage cannot be found between the placenta and uterus. In this series, when a cleavage plane was absent, all the placentas revealed some degree of accreta when examined microscopically. Furthermore, not a uterus was removed which did not show some evidence of accreta. Hence, we feel that the term "adherent placenta" is a misnomer.

*This apparently irreducible morbidity rate should warrant consideration of the prophylactic administration of parenteral sulfadiazine or penicillin in all cases where manual removal is necessary. Unfortunately, the offending organism is the anaerobic streptococcus. We have found that the early use of Elliott treatments is most effective in this type of infection.

When the diagnosis of placenta accreta is made, irrespective of type, no further attempt should be made to remove the placenta pelvically, but an immediate supravaginal hysterectomy should be done. It could be argued that many of the patients with focal and partial accretas could be treated successfully by the vaginal route. That such a method of treatment is resorted to in most clinics must account for the absence of accretas in other papers on manual removal, compared with the high incidence encountered in this series. We feel that in some of the maternal deaths said to be caused from hemorrhage and shock which occurred in cases where difficulty was encountered in establishing a cleavage plane, the operators actually were dealing with patients who had focal or partial placenta accreta. The only two deaths in this series resulting from hemorrhage and shock were associated with such conditions. One patient had a partial accreta, while the other patient had multiple areas of focal attachments. When the affected portions were forcefully removed, severe hemorrhage resulted from the rupture of the coherent maternal sinusoids. Although uterine packing was immediately performed, both patients were in irreversible shock by the time hysterectomies could be performed. Heroic measures at blood replacement were of no avail, and both patients died. Such catastrophies should emphasize the immediate dangers which are present even when the degree of accreta is minimal. Conversely, there is undoubtedly less risk to the patient who has a complete placenta accreta, because the operator probably will be unable to dislodge the placenta, and, therefore, will perform an immediate hysterectomy. Moreover, we believe that many of the delayed hemorrhages in the puerperium and probably many of the cases with a "placental polyp" are the results of partial or focal placenta accreta which were unrecognized at the time of manual removal. A certain number of these patients will subsequently demand radical measures before the vaginal bleeding can be properly controlled.

These experiences have proved to us that a definite plan of treatment should be carried out in all cases of placental retention. Within one-half to one hour following delivery, a diagnosis of a retained placenta should be made. Preparations should ensue for immediate manual removal. We believe very strongly that this operation should be carried out in an operating room equipped for an immediate laparotomy, as well as for manual removal. After the patient is anesthetized, a Credé expression should always be tried. If this procedure fails, manual removal should immediately be attempted. Uterine packing should be resorted to if there is any question that the uterus is not contracting properly.

If a placenta accreta is encountered, the uterus should be packed at once with sulfanilamide gauze and an immediate supravaginal hysterectomy be performed. The pack is removed, vaginally, prior to amputation of the cervix. The amount of hemorrhage is markedly reduced by this method. Usually, ten grams of sulfanilamide powder is placed under the peritoneal flap covering the cervical stump. Multiple trans-

fusions are usually necessary when the blood loss has been great. In this manner, we believe we should be able to reduce further the mortality arising from shock and hemorrhage associated with either uterine atony or faulty implantation of the placenta in patients who demand manual removal.

Conclusions

1. An analysis of 217 cases of manual removal of the retained placentas following the delivery of a viable infant is reported. This operation was necessary once in every 210 deliveries.

2. The gross mortality rate is 1.8 per cent, and when corrected, is 1.3 per cent.

3. The gross morbidity rate is 28.8 per cent, and when corrected, is 24.1 per cent.

4. The morbidity rate is markedly increased by the following factors (Table X):

- (a) A blood loss exceeding 500 cubic centimeters.
- (b) A placenta allowed to remain in the uterus more than two hours following delivery.
- (c) The necessity for uterine tamponade.
- (d) Associated placenta accreta.

TABLE X. SUMMARY OF FACTORS

FACTORS	TOTAL CASES	AVERAGE BLOOD LOSS, C.C.	MORBIDITY	
			NUMBER OF CASES	PER CENT
Blood loss over 500 c.c.	88	786	35	38.6
Placenta retained over 2 hours	76	608	31	40.7
Uterine tamponade	18	933	10	55.5
Placenta accreta	24	1041	14	58.3

5. Placenta accreta occurred in 11.0 per cent of all cases. We believe such cases are best treated by abdominal supravaginal hysterectomy, rather than by the pelvic route.

6. A policy of treatment in manual removal of the placenta is presented. We believe this policy will further reduce the number of deaths from shock and hemorrhage.

References

- Goethals, T. R.: AM. J. OBST. & GYNEC. 6: 322-332, 1923.
- Peckham, C. H.: Bull. John Hopkins Hosp. 56: 224-235, 1935.
- Schwartz, H. A., and Richards, W. R.: AM. J. OBST. & GYNEC. 45: 235, 1943.
- Irving, F. C., and Hertig, A. T.: Surg., Gynec. & Obst. 64: 178-200, 1937.
- Hertig, A. T.: Personal communication.
- Irving, F. C.: A Textbook of Obstetrics for Students and Practitioners, New York, 1936, Macmillan Co.

NONINVOLUTION OF THE PLACENTAL SITE

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THE extreme efficiency with which the postpartum uterus solves its own problems of hemostasis, of reduction in bulk, and of return to the nongravid state readied for subsequent reimpregnation, is noteworthy. The mucosal surface of the postpartum uterus is recovered within the first 14 days, and often at an even more rapid rate. The necrotic slough has been cast off by this time and the gland stubs have served as the hub from which the new epithelial covering springs. The bulk of the uterine muscle is reduced sharply either by loss of cytoplasm of the individual cells, or by actual loss of cells by autolysis, or by fatty degeneration.

Important in this process are the blood vessel changes, notably in the postpartum uterus. A physiologic obliteration takes place as the arteries undergo obliteration and hyaline degeneration, whereas the veins undergo thrombosis with subsequent organization. With increasing parity, there is increased elastic tissue around the blood vessels due largely to incomplete or imperfect absorption during the puerperium, as Shaw's¹ studies emphasize. Goodall² has found that new blood vessels are formed within the lumina of the old blood channels in subsequent pregnancies. Schwarz³ has confirmed these views and adds that in the more marked grades of subinvolution, masses of incompletely absorbed, dead, swollen elastic tissue are found between the muscle bundles.

Williams⁴ has found that the placental site is handled in such fashion as to leave a minimal scar upon the uterine mucosa. The placental site is exfoliated by a process of growth of the new endometrium from beneath the site, as well as by ingrowth from all sides. This requires six weeks or even longer in contrast to the more rapid rate of mucosal surfacing. This process apparently is designed to prevent scarring of the endometrium with each pregnancy—otherwise, increasing parity ultimately would ablate any further possible sites for implantation of the fertilized ovum. After six weeks, it is virtually impossible to detect microscopically the placental site.

Schwarz has described the microscopic picture of the subinvolted uterus as one with an increased amount of elastic tissue around the blood vessels and between the muscle bundles, together with the formation of new blood channels within the lumina of the degenerated and obliterated vessels. Clinically, this uterus, which is seen by the gynecologist more frequently than by the obstetrician, is one larger than normal. Its consistency is soft and boggy. Characteristically, its cut surface is made irregular by projections of thickened blood vessels. The pa-

tient's complaints are often those of bleeding, discharge, discomfort. Described with this is chronic endometritis associated with malpositions of the uterus or infections elsewhere in the pelvis.

Well known, too, is the entity of retention of bits of placental tissue and its clinical pattern of bleeding, failure of uterine involution often requiring operative intervention.

It is the purpose of this brief report to emphasize the fact that there may be failure of involution of the placental site itself without the associated picture of subinvolution as it has been described, or without the retention of placental tissue. This would represent failure of the physiologic process of obliteration of the large vessels underlying the placental site. Varying degrees of failure will be apparent in the attached case reports.

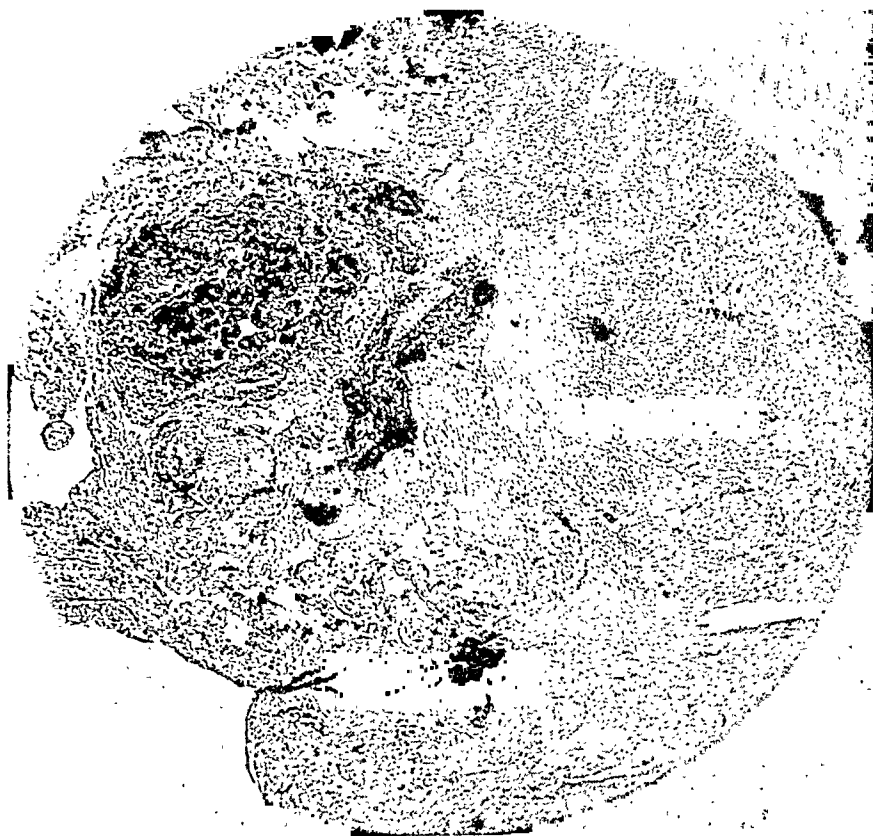


Fig. 1.—Case 1. Low-power view of placental site tissue with placental site giant cells, a hyalinized stroma which is infiltrated by chronic inflammatory cells and a few hemosiderin-laden macrophages. Vessels are but partially obliterated.

Case Reports

Three cases will be presented from the Boston Lying-in Hospital. Each may be noted as a clinical variant of the picture of noninvolution of the placental site, but coming at different periods in the puerperium.

CASE 1.—MRS. C. D. (B.L.I. 96262) is a 29-year-old para i, who was delivered without event as a breech. The uterus contracted well following delivery. The placenta and membranes were complete. Her postpartum course was uneventful with a physiologic amount of lochia.

On the tenth postpartum day, her uterus had involuted to twice normal size and she was discharged without complaint from the hospital on her twelfth postpartum day. From discharge onward, the patient continued to flow, using 2 to 3 pads daily, without cramps. On the day of entry, 6 weeks postpartum, she gushed suddenly and painlessly an estimated cupful of bright blood. She was not lactating.

On examination, the uterus was one and a half times normal size, the os would admit a finger. No other abnormalities were found. Upon both dull and sharp curettage, only a small amount of endometrium was obtained, the total measuring 1.5 by 1.5 centimeters. The patient stopped bleeding and her puerperium was completed with no more flow.

On microscopic examination, no placental tissue could be found. The endometrium was atypical secretory in nature. Placental site tissue was found with placental site giant cells and a few hemosiderin-laden macrophages. Vessels in this area were but partially obliterated. (Fig. 1.)

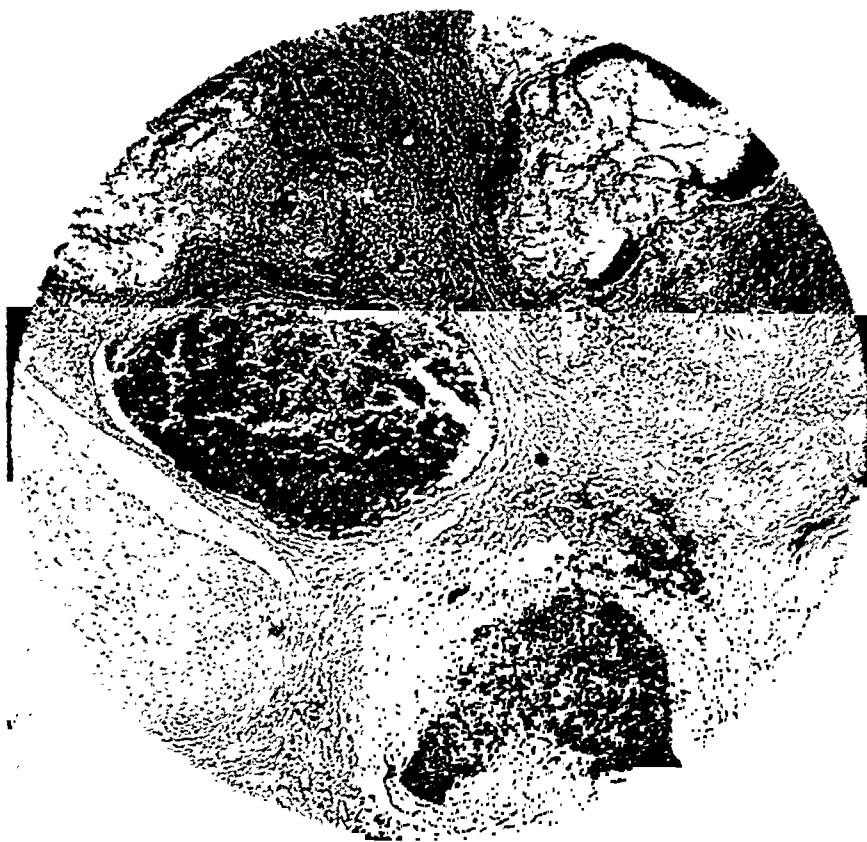


Fig. 2.—Case 2. Low-power view showing numerous patent blood vessels of the placental site. This demonstrates failure of the usual mechanism of thrombosis and organization or by endarteritic obliteration. There is intense subacute and chronic inflammatory cell infiltration, with some placental site giant cells. No villous structures are seen.

CASE 2.—Mrs. C. B. (B.L.I. 95791) is a 38-year-old para vii, whose previous pregnancies had been normal. The present pregnancy was complicated by a 10 cm. fibroid mass, which rose out of the pelvis early in pregnancy, but caused no further trouble. After an easy labor, the patient delivered normally and had an uneventful puerperium, flowing only the physiologic amount. The placenta and membranes were complete. On the day of discharge at 11 days postpartum, the uterus was

twice normal size, in good position, with the os closed. Two days later, on the thirteenth postpartum day, the patient began to bleed at home an estimated 5 to 6 pads, but this responded to oral ergotrate gr. $\frac{1}{320}$ thrice daily. However, two days later, the patient again began to bleed despite the oral ergot preparation, and required hospital admission for blood loss which was estimated at 500 cubic centimeters. On admission, 15 days postpartum, the patient was in fair condition with a pulse of 90, a blood pressure of 136/80. The uterus was thrice normal size, the os was 2.5 cm. dilated. Curettage was performed using both dull and sharp curettes, obtaining a mass of tissue measuring 4 by 3 by 3 centimeters. The patient bled no more and her puerperium ran out a subsequent normal course.

On microscopic examination, first as a frozen section, numerous patent blood vessels of the placental site were found demonstrating failure of thrombosis and organization. Some were visible grossly. On permanent section, the curettings demonstrated hemorrhage and necrosis of the decidua, some of which contained enormously enlarged vessels (probably relatively enlarged by contrast with involution of the surrounding tissue), with improper and poor obliteration of their lumina by the endarteritic and thrombotic process. Some myometrium also was present which contained extremely large vessels and a few placental site giant cells. For the most part, the picture was one of intense sub-acute inflammation associated with subinvolution or noninvolution of the placental site. No villous structures were seen. (Fig. 2.)

CASE 3.—Mrs. M. H. (B.L.I. 94716) is a 29-year-old para viii. This pregnancy was complicated by intermittent bleeding throughout the middle trimester, which was found to have been due most likely to a placenta circumvallata found at delivery in the patient's home. The placenta and membranes were complete. Following the last of her previous 5 full-term pregnancies, the patient flowed for 8 weeks and had required curettage. No microscopic diagnosis could be obtained from that hospital. Following the present pregnancy, she began to flow the usual amount of lochia, but continued for the next 21 days, using 6 to 8 pads daily even though on bed rest and oral ergot preparations. At the end of this time, the patient was admitted to the hospital because of continued bleeding and weakness. The uterus on examination was twice normal size, the os admitted a fingertip. The patient was curetted with both dull and sharp curettes, obtaining a mass of tissue measuring 2 by 1.5 by 0.5 centimeters.

Microscopic examination revealed endometrium composed for the most part of orderly and regularly arranged glands in the early proliferative phase, showing nuclear pseudostratification with some mitotic activity. The supporting stromal cells were naked. In areas, there was considerable necrosis with a few cells of the decidual type apparent. There were numerous large vessels in the myometrium and in the supporting stroma which were thrombosed. Some of them, however, showed lumina which were not yet completely obliterated. There was minimal inflammatory cell infiltration. The myometrium was composed of regularly arranged bundles of smooth muscle cells. Some of the cells were quite swollen and still showed pregnancy changes. Placental site was still apparent.

After curettage, the patient continued to bleed using 4 to 8 pads daily. Bed rest and ergot therapy were still without effect. After continued observation for 8 days, with no cessation in bleeding, a supravaginal

hysterectomy was performed. Convalescence was smooth following operation.

On gross examination, the uterus measured 8 by 8 by 6 centimeters. Upon opening the uterus, there was found an adherent mass on the anterior uterine wall. This measured 5 by 2.5 by 1.5 cm., and was composed of partially organized blood clot and necrotic material difficult to identify.



Fig. 3.—Case 3. Photograph of the microscopic slide in Case 3 demonstrating the adherent mass on the anterior wall. This represents noninvolved placental site intermingled with blood clot. The underlying vessels are incompletely obliterated, although a few are filled with organizing blood clot or hyalinized material. The superficial endometrial layer has grown to cover partially this polypoid mass, which is yet adherent to the uterine wall by only a very small pedicle. There are a few hyalinized or ghost villi left, suggesting some retained placental tissue.

On microscopic examination, the endometrium of the general uterine cavity was completely repaired, showing nuclear pseudostratification and some mitotic activity in the superficial layer. The supporting stromal cells were naked of cytoplasm. The adherent mass described grossly was found to be a noninvolved placental site with intermingled blood clot, and with a few hyalinized villous structures present as well. The underlying vessels, both the decidual sinusoids and the spiral arterioles, show varying degrees of thickening of the vessel walls, and some are obliterated by organizing thrombus or by hyalinized material. More vessels, however, are incompletely obliterated with erythrocytes still free within their lumina. The superficial endometrial layer has grown to cover partially this polypoid mass, which is yet adherent to the uterine wall by only a very small pedicle. (Fig. 3.) The picture is one of noninvolution of the placental site associated with a remnant of placental polyp.

Sections taken from the lower uterine segment showed no alteration in their normal architecture. The supporting myometrium was composed of regularly arranged bundles of smooth muscle cells. The serosal surface was intact. A few lower segment glands were present.

Discussion

These cases were selected to demonstrate the varying clinical pictures possible during the early puerperium due to noninvolution of the placental site. The process of physiologic obliteration of the vessels of the gravid uterus is a generalized one, but it is most marked in the region of the placental site. It is in this area of placental attachment where one would suppose the maximal numbers of blood vessels would occur. Elsewhere in the uterus, the surface epithelium regenerates rapidly and the vessels are but a minor part of the picture. In the placental site, however, the whole area is extruded, as it were, along with the bulk of its obliterated vessels. This pinching off process requires an average of 6 weeks, as Williams has shown, and is completed by an undergrowth of endometrium from all sides, as well as from beneath the placental site. As a consequence of the magnitude of the process, the sequence of obliteration of vessels, slough and extrusion of the placental site takes not only longer, but if incomplete, carries a much greater bleeding potential than the simpler regression elsewhere in the uterus.

Generalized failure of involution prolonged beyond the normal limits has been described as subinvolution of the uterus. We are not dealing with that entity in these cases, for this problem is one in the early weeks following delivery. In these cases, the physiologic regression of muscle and vessels takes place properly in all spots but the placental site. In the third case presented (Fig. 3), the endometrial surfacing had covered even polypoid placental site, as well as endeavoring to undergrow it. This truly seems a localized failure rather than the generalized picture known as chronic subinvolution.

Neither is this the picture of placental polyp, although in the last of the three cases some hyalinized "ghost" villi were yet apparent within the mass of placental site tissue. The true placental polyp has viable tissue in addition to these "ghost" structures.

Certainly subclinical variations of this picture are seen—the case which clears up on ergot and bed rest at home after bleeding small amounts only for some period of time. This case does not require curettage. Case 1 illustrates that this problem can exist in the primipara, rather than to accept it as a function of multiparity. It would seem more likely to occur, however, in multipara because of the very nature of the process. In Case 3, the patient undoubtedly had noninvolution of the placental site with her last pregnancy, for this, too, had required curettage. With the present pregnancy, she developed a more severe degree of the same picture.

Curettage seems to be an easy, effective treatment. It would have been satisfactory in Case 3, had not the curette missed the small area of attachment of the placental site to the uterine wall.

Summary and Conclusions

1. Three cases are presented in clinical and pathological detail to illustrate the entity of noninvolution of the placental site.

2. Such a problem is one belonging to the early weeks of the puerperium rather than existing as a chronic state of generalized incomplete uterine involution—"chronic subinvolution of the uterus."

3. There seems to be failure of complete physiologic obliteration of the placental site vessels so that hemorrhage accompanies the casting off of the placental site. This is in contradistinction to placental polyps. Chronic inflammation plays but little part in these cases.

4. Treatment consists of the usual ergot preparations and bed rest. Failing this, curettage should be curative.

5. It would seem that this is more likely to occur in multipara, and that there may well be a tendency for this problem to appear in subsequent pregnancies.

Dr. Frederick C. Irving is to be thanked for his criticism of the manuscript.

References

1. Shaw, W. F.: *Obst. Trans.*, London, 1907.
2. Goodall, J. R.: *Studies from the Royal Victoria Hospital, Montreal*, Vol. 2, No. 3, *Gynecology* ii, 1915.
3. Schwarz, O. H.: *Am. J. Obst.* 79: 63-94, 1919.
4. Williams, J. W.: *J. A. M. A.* 97: 523-528, 1931.

THE INFLUENCE OF STILBESTROL UPON LACTATION

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STILBESTROL is being employed as an aid in suppressing lactation. During its administration, the infant is not placed at the breast. Since the treatment is employed in the absence of nipple stimulation, certain questions arise: (a) Is the suppression of lactation primarily the result of the medication, or (b) is it due to the withdrawal of the nipple stimulation?

Abarbanel and Goodfriend¹ and Karnaky² deny that stilbestrol will depress lactation in the presence of normal nursing.

Stewart and Pratt,³ Diddle,⁴ Davis⁵ and Connally⁶ reported that stilbestrol will inhibit lactation in spite of normal nursing.

Because of this difference of opinion in the literature, we wish to present certain results of our investigations.

Material and Methods

This study is based on observations upon a series of 250 patients, who were delivered in the Hospital of the University of Pennsylvania between January, 1940 and January, 1942.

The effect of stilbestrol upon lactation was observed in 4 groups of patients under the following conditions:

- A. In absence of nursing; no pumping of breasts.
- B. In absence of nursing; with pumping of breasts.
- C. Following short period of nursing.
- D. During nursing.

In groups A and C, the effect of stilbestrol upon lactation was measured in terms of its influence upon breast discomfort, engorgement, leakage during treatment, and leakage after discontinuation of stilbestrol. In groups B and D, the effect of treatment was recorded as ounces of milk obtained by pumping, or grams of milk taken by the infant.

The nursing routine included nursing on alternate breasts for 20 minutes, every 4 hours. Breasts were supported properly, fluid intake was encouraged, and strenuous catharsis was omitted. Mothers were given specific instructions as to how to nurse properly, and how to keep the breasts clean and well supported.

The routine treatment for each group was as follows:

- 1. Fluid intake at least 3,000 c.c./24 hours.
- 2. No unusual cathartics.
- 3. Support of breasts—no tight binders.
- 4. Stilbestrol 1 mg., three times daily for 5 days.

A. Treatment in Absence of Nursing—No Associated Pumping of Breasts.—

Stilbestrol was given to 50 patients who did not nurse at any time,

and whose breasts were not pumped. Treatment was started within 48 hours of delivery, with the results shown in Table I.

TABLE I. TREATMENT IN ABSENCE OF NURSING—NO ASSOCIATED PUMPING OF BREASTS—50 PATIENTS

	PATIENTS
1. Breast discomfort	0
2. Engorgement	0
3. Leakage during treatment	0
4. Leakage after discontinuation of treatment	5
5. No symptoms	45
Total	50

B. Treatment in Absence of Nursing—With Associated Pumping of Breasts.—

Fifty patients did not nurse at all but were pumped at regular intervals beginning 48 hours after delivery. An electric breast pump was used at 4-hour intervals on alternate breasts. As soon as 8 ounces of milk were secured per 24 hours, stilbestrol treatment was begun and continued simultaneously with pumping for 5 days. The results are shown in Fig. 1. Note the drop in milk secretion within 24 hours of the start of stilbestrol administration, and the continuing decrease as long as the drug was administered.

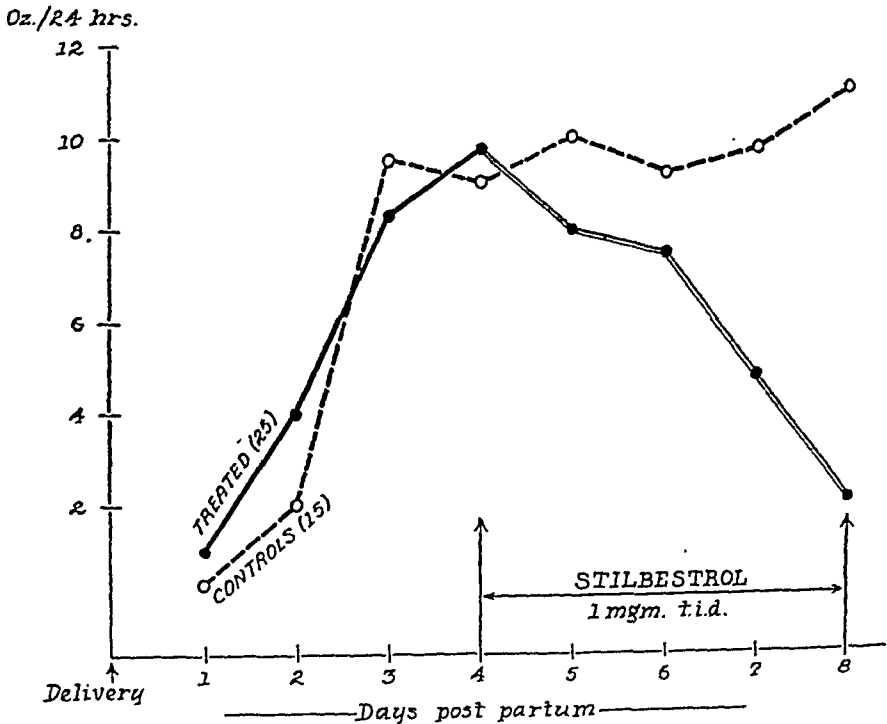


Fig. 1.—Effect of stilbestrol upon lactation. Nipples stimulated by pumping breasts during administration of drug.

C. Treatment Following Short Period of Nursing.—

The effect of stilbestrol upon lactation after it is well established was observed in 50 patients, who had nursed for 5 days or longer, but stopped nursing because of neonatal illness or death. As soon as the patients ceased nursing, the routine treatment for drying up breasts

was instituted. The nipples were not stimulated by pumping or suckling during the period of stilbestrol treatment. The results are shown in Table II.

TABLE II. TREATMENT FOLLOWING SHORT PERIOD OF NURSING—50 PATIENTS

	PATIENTS
1. Breast discomfort	7
2. Engorgement	7
3. Leakage during treatment	3
4. Leakage after discontinuation of treatment	4
5. No symptoms	29
Total	50

The discomfort, engorgement, and leakage during treatment lasted no longer than 36 hours in any case, and no treatment was needed because these symptoms were so mild. The cases of leakage after discontinuation of stilbestrol were relieved by additional 5-day courses of the drug. The longest interval between the 2 courses of stilbestrol was 2 weeks; this occurred in one case.

D. Treatment During Normal Nursing.—

This group consisted of 100 normal nursing women who previously had nursed at least one infant for three months. All of the present pregnancies and deliveries were uneventful. All infants were normal and weighed at least 3,000 grams at birth. In most instances, the mothers did not know they were under treatment.

Since we were anxious to study the effect of stilbestrol upon the amount of milk produced daily, it was measured in terms of: (1) daily infant weight, and (2) milk taken by each infant at each feeding.

(1) *Daily Infant Weight.*—Twenty patients were treated and twenty were used as controls. In the control group, the mothers nursed their infants normally.

In the treated group, as soon as the infants began to gain weight after their initial neonatal weight loss, the mothers were started on 1 mg. of stilbestrol, three times a day for 3 days.

The infants in both groups were weighed daily at the same time. They were undressed completely at the time of each weighing.

None of the infants exhibited anorexia, vomiting, vaginal bleeding or unusual breast hypertrophy.

Results

These are shown in Fig. 2. Note that the infant weights in the treated group remained stationary during the period that the mothers were receiving stilbestrol. After the drug was discontinued, the infant weight increased, so that at the time of discharge from the hospital the average weight in the treated group was comparable to that of the control group.

(2) *Milk Taken by Each Infant at Each Feeding.*—This group included 40 treated women and 20 controls. After the infants were obtaining at least 200 grams of milk per 24 hours from the mothers, treatment was instituted. Stilbestrol was administered in doses of 1 mg., three times daily for 4 days. The infants were given no supplementary feedings during the experimental period.

The mothers were not advised of the experiment, although they received special instructions as to proper nursing—with emphasis upon the

importance of encouraging the infant to empty the breasts as completely as possible at each feeding.

Results. These are shown in Fig. 3. Note the drop in milk obtained by infants from treated mothers as compared to the amount of milk procured from untreated mothers.

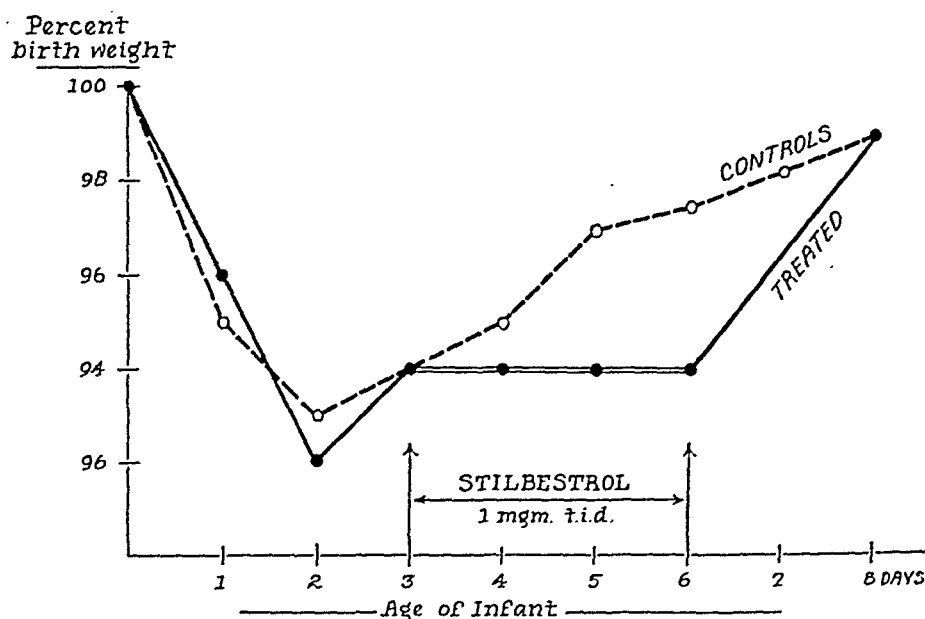


Fig. 2.—Effect of stilbestrol upon weight of infant. Drug administered to nursing mothers after onset of lactation.

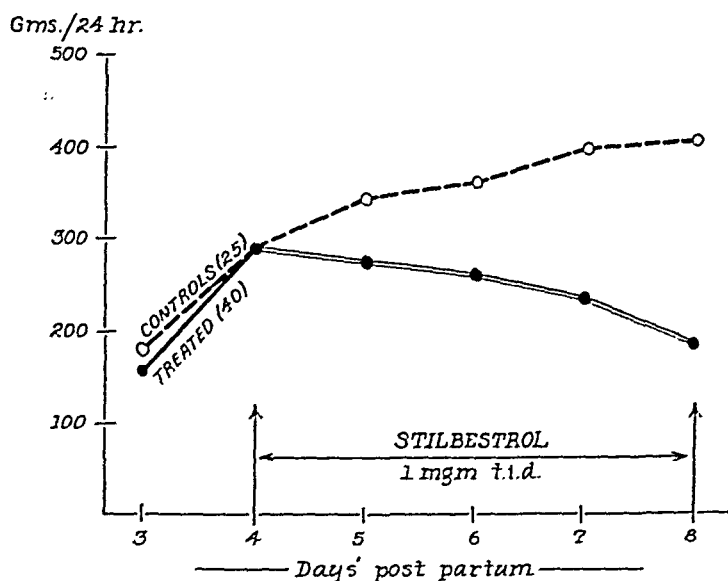


Fig. 3.—Effect of stilbestrol upon lactation. Nipples stimulated by normal suckling during administration of drug.

During the period of treatment, many mothers complained that their infants seemed hungry and would always cry. The mothers felt that they did not have enough milk for their babies.

After treatment was discontinued, most of the treated group of mothers were able to nurse their infants satisfactorily within 3 days.

Discussion

Several interesting points arose during our experiment. First, the effect of stilbestrol upon lactation is not the same in every postpartum patient. Some were affected very slightly, while others showed a marked response to the drug in the same dosage. In fact, the usual means of mensuration, that is weighing the infant before and after each feeding, occasionally failed to demonstrate any decrease in milk secretion as illustrated in Fig. 4. From the onset of lactation, this patient was noted to have a superabundance of milk, and after the infant finished nursing, the breasts continued to leak. They were

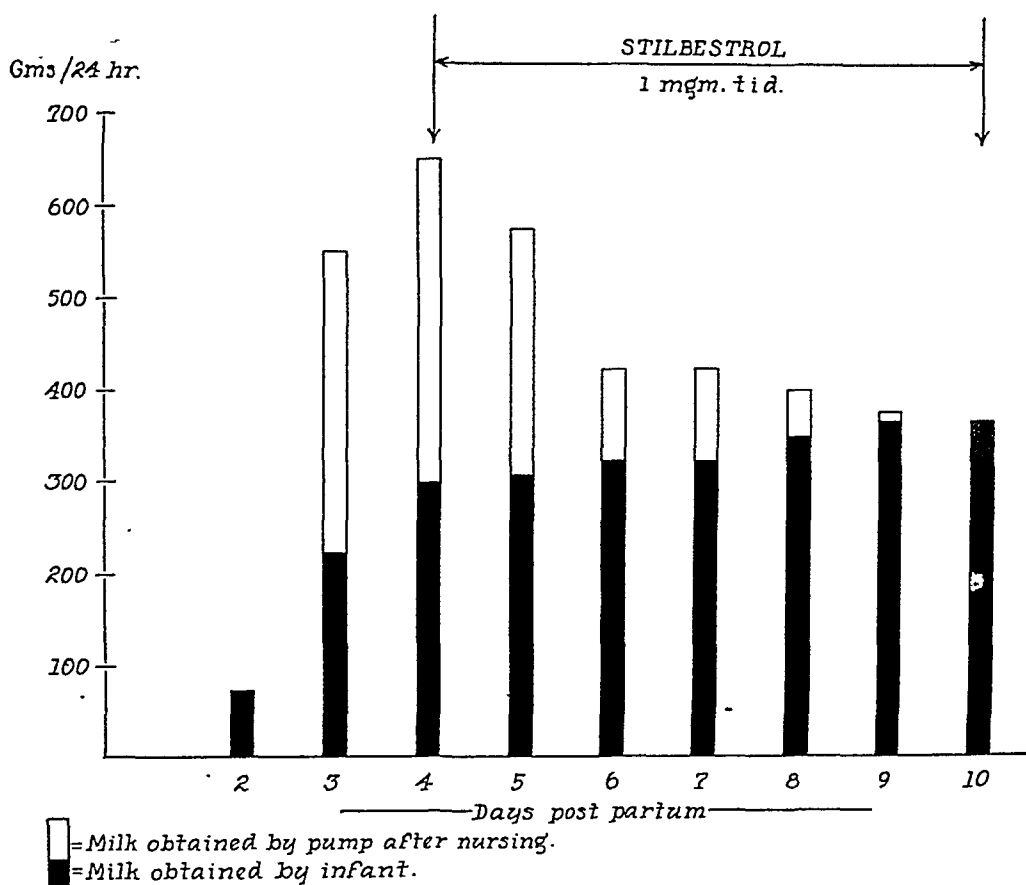


Fig. 4.—Effect of stilbestrol upon total amount of milk produced by mother.

pumped, and between 200 and 300 grams of milk were obtained in this manner after nursing. The amount of milk that was produced by this patient, as judged from the daily infant weight gain, seemed to be increasing in spite of the stilbestrol. According to routine records obtained by weighing the baby before and after nursing, this infant continued to take increasing amounts of milk in spite of the administration of stilbestrol to the mother; yet the amount of milk obtained by pumping after each nursing decreased to zero soon after stilbestrol was started. This observation may explain why some patients show no effect of stilbestrol on lactation during nursing.

In the other patients in our series, this type of observation was not possible because the breasts were readily "emptied" by the infant. In many cases we tried to pump the breasts after the infant had finished nursing, and practically no milk was obtained.

Another interesting point brought out by our study is the absence of a quantitative relationship between dose of stilbestrol and effect on lactation. We found that 1 mg. three times daily produced the same degree of depression in milk secretion as 20 mg., four times daily. Table III demonstrates this point clearly.

TABLE III. INFLUENCE OF STILBESTROL UPON LACTATION
EFFECT OF DOSAGE

TREATED PATIENTS (40)				
NO. IN EACH GROUP	TREATMENT		MILK SECRETION (ON 8TH POSTPARTUM DAY)	
	AMOUNT TOTAL MG.	DURATION DAYS	GM. (AVERAGE)	% DEPRESSION
15	36	4	186	54
10	56	5	160	60
6	203	6	160	60
9	426	5.5	170	58
CONTROLS (25 NORMAL POSTPARTUM WOMEN) 408				

Showing the relative amount of milk secretion on the last day of postpartum treatment by patients receiving stilbestrol, compared with the average amount secreted on the eighth postpartum day by the control group.

NOTE: (a) Depression of milk secretion following treatment. (b) That there is no direct relationship between amount of drug given and degree of depression of milk secretion.

The other point of interest is the ability of postpartum women to take varying doses of stilbestrol by mouth with no demonstrable untoward effects. None of the mothers or infants in our series showed any unusual signs or symptoms that could be attributed to the stilbestrol.

Summary and Conclusions

The effect of stilbestrol upon lactation was studied in 250 normal postpartum women under 4 types of circumstances, with the following conclusions:

1. Stilbestrol is effective in aiding cessation of lactation.
2. Stilbestrol given to normally nursing postpartum women will depress milk secretion in spite of normal suckling.
3. In rare cases, stilbestrol may have no obvious effect upon lactation.
4. The dose of stilbestrol bears no quantitative relation to its effectiveness in depressing milk secretion.

References

1. Abarbanel, A. R., and Goodfriend, M. J.: AM. J. OBST. & GYN. 40: 1037, 1940.
2. Karnaky, K. J.: Ibid. 41: 565, 1941.
3. Stewart, H. L., Jr., and Pratt, J. P.: Ibid. 41: 555, 1941.
4. Diddle, A. W.: Ibid. 41: 563, 1941.
5. Davis, M. E.: Ibid. 41: 564, 1941.
6. Connally, H. F., Jr.: Ibid. 46: 125, 1943.

THE CATHETER METHOD FOR CONTINUOUS CAUDAL ANESTHESIA

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THE introduction of continuous caudal anesthesia in obstetrics by Edwards and Hingson has elicited widespread interest, and as a result, a number of modifications of their original technique have been reported. One of these is the employment of a ureteral catheter instead of an inlying steel needle for the administration of the anesthetic substance.

In 1942, Manalan¹ described his method for single injections, and in 1943, Adams, Lundy and Seldon^{2, 3} reported their observations on the use of an inlying ureteral catheter for continuous caudal anesthesia. Siever and Mousel,⁴ who used a 13 gauge needle and a No. 5 ureteral catheter, reported satisfactory results in 96 per cent of their series of 300 obstetric patients. Irving,^{5, 6} employed a 15 gauge needle and a No. 4 catheter, and for difficult insertions used an 18 gauge needle as a guide with a 15 gauge needle slipped over it.

This report describes our procedure, which differs from other methods previously reported in that a wire guide is used to facilitate the introduction of the catheter.

Method

Indications.—Caudal anesthesia for obstetric patients is instituted only when labor has made definite progress. The primiparous cervix should be dilated at least 4 cm., while 2 to 3 cm. is sufficient in the multiparous patient. Uterine contractions in *all* instances should be at intervals of 3 minutes or less.

Preliminary Preparation.—Premedication with a barbiturate—usually 3 grains of nembutal or seconal are given 15 minutes beforehand. The bladder is emptied, and the large bowel cleansed with a low enema.

Technique.—The patient is placed face down with the hips elevated by a large pillow. The sacral region is painted with tincture of phenol or merthiolate and draped with sterile towels. The sacral hiatus is identified and a wheal is raised in the overlying skin with local anesthetic solution. Metycaine, 1.5 per cent, has proved satisfactory. A 22 gauge 2-inch needle is connected to the syringe and passed through the skin wheal and the sacrococcygeal ligament into the caudal canal. When the caudal space is entered, a characteristic "jump" is felt as the needle point traverses the depth of the caudal canal and strikes the anterior wall.

Five c.c. of 1.5 per cent metycaine solution are injected to serve as a test for undue reaction, and to render the remaining portion of the procedure painless. The needle is removed and a 15 gauge 3-inch needle

is introduced, bevel-up, into the canal. As soon as the sacrococcygeal ligament is penetrated (this is readily discerned with the rigid needle), the hub is depressed and the needle advanced for a distance of 5 to 6 centimeters. It is important to avoid scraping the anterior wall of the canal, where many blood vessels may be encountered.

The bevel of the needle is now directed downward and the stilet removed. If neither blood nor spinal fluid can be aspirated, an additional 5 c.c. of metycaine is injected, and if the 15 gauge needle is in proper position, it will flow in easily.

An autoclaved No. 4 ureteral catheter with wire guide is now made ready for insertion. The wire guide remains in the catheter, but *before insertion* it is withdrawn for a distance of 2 cm. from the catheter tip. This retains the advantage of the guide, while providing a soft, flexible tip which is not likely to penetrate the dura or blood vessels.

The catheter is passed through the needle until its tip is 3 to 4 cm. beyond the needle point. The needle is withdrawn over the catheter and the depth of insertion adjusted. The catheter may be advanced or withdrawn at this juncture as long as the guide has not been removed. The average patient requires a depth of 12 cm., while 10 cm. will suffice for a thin person. Obese patients must have the catheter inserted 15 cm. to insure its remaining in the canal. Distances are from the catheter's exit at the skin and are easily determined with a calibrated catheter.

The wire guide is now withdrawn and the catheter strapped firmly in place with adhesive tape. A 22 gauge $\frac{3}{4}$ -inch short-bevel needle is inserted into the distal tip of the catheter and aspiration attempted with a syringe. If neither blood nor spinal fluid appears the needle is connected by means of a Luer-Lok fitting to a rubber tube leading to the metycaine bottle. A two-way automatic valve and a 10 c.c. syringe complete the closed system.

Fifteen c.c. of metycaine are injected through the catheter, making a total initial dosage of 25 cubic centimeters. This often suffices to relieve all uterine pain and produce skin anesthesia up to the umbilicus. If not, 10 to 15 c.c. more may be injected. Subsequent injections of 20 c.c. are given, whenever the patient feels her pain returning. The skin level of anesthesia is best maintained at, or slightly below, the umbilicus.

Observations and Precautions

1. *Stage at Which Caudal Anesthesia Is Instituted.*—As emphasized by McCormick,⁷ it is most practicable to delay institution of caudal anesthesia until labor is well advanced and the pains are at 2- to 3-minute intervals. This is advantageous because it forestalls the necessity of discontinuing the procedure because contractions have stopped. It also shortens the duration of anesthesia, thus diminishing the total dosage and reducing the possibility of a toxic effect on mother or baby.

2. *Use of the 15 Gauge Needle.*—The needle point must avoid the anterior wall of the caudal canal or troublesome bleeding will ensue. The rigid needle is more readily controlled than one of malleable construction.

Test aspirations for blood or spinal fluid should be made with the needle in both bevel-up and bevel-down positions. The needle should be rotated to the bevel-down position *before* introducing the catheter as a precaution against shearing the catheter tip. This occurred once

in our series. The needle was bevel-up and a 1 cm. piece was cut off by the sharp, up-turned bevel. At the patient's request, no attempt was made to recover the tip, and she has experienced no ill effect. We believe such an accident is less likely to occur if the needle is bevel-down when the catheter is inserted.

When the 15 gauge needle and the catheter are *both* in the caudal canal, there are two things to avoid: (1) the needle *must not* be inserted farther, and (2) the catheter *must not* be withdrawn until the needle has first been removed. Either of these tends to shear the catheter.

3. *Use of the Ureteral Catheter.*—It is unsafe to insert the catheter with the wire guide *without first withdrawing the guide* 2 cm. from the catheter tip. If this precaution is not observed the subarachnoid space will surely be entered.

Test aspirations for blood or spinal fluid *must* be made through the catheter after it has been placed. In spite of all precautions, we have aspirated blood a number of times and spinal fluid once.

4. *Asepsis.*—Scrupulous care must be taken in the sterile preparation and draping of the sacral area. Sterile gloves should be worn by the operator, and subsequent injections must not contaminate the syringe piston.

5. *Level of Skin Anesthesia.*—The catheter method produces higher levels of skin anesthesia than are obtained with the needle. For this reason, the initial injection should not exceed 25 cubic centimeters. If necessary, this may be increased until the skin level is at the umbilicus. Several of our earlier catheter caudal blocks produced skin anesthesia to the clavicles. One patient experienced numbness of the arm and hand, but there appeared to be only slight paralysis of the intercostal muscles. This has not occurred since limiting our initial dosage to 25 cubic centimeters.

6. *Prevention of Urinary Distention.*—If the anesthetic is continued for longer than 6 to 8 hours, the bladder must be catheterized. Frequently, it may be emptied by gentle suprapubic pressure with the patient on a bedpan. This precaution is especially important in preventing postpartum cystitis and urinary retention.

7. *Barbiturate Administration.*—It is generally accepted that barbiturates lessen the toxicity of the local anesthetic agents. It is probably well to repeat the nembutal or seconal at intervals of 6 to 8 hours, to offset loss of the drug's effect by metabolism.

8. *Excessive Drop in Blood Pressure.*—Although this occurred in not more than 2 per cent of our patients, measures for control are kept at hand. Administration of oxygen is of most benefit, but neosynephrine and ephedrine are good.

Results

Satisfactory anesthesia was obtained in 277 of our first 300 unselected cases, and there were only 6 (2 per cent) complete failures. Twenty-three (8 per cent) required supplemental anesthesia. Light supplemental anesthesia was administered to an additional 26 patients, because they wished to be asleep in the delivery room. With 2 exceptions, the caudal blocks were administered by 7 different members of our resident staff.

Nine cesarean sections and 5 gynecologic operations are included in our series. The remaining 286 are vaginal deliveries consisting of 10

spontaneous, 251 low forceps, 7 midforceps, 2 high forceps, 12 breech, and 4 version and extraction cases. Each of the last 4 necessitated deep inhalation anesthesia to provide sufficient relaxation of the uterus.

There were no maternal deaths. Seven babies were lost, a fetal mortality of 2.4 per cent, but none of these was attributable to the caudal block.

Complications resulting from the caudal anesthesia occurred in 2 patients. A superficial skin infection developed at the site of the catheter's exit in one, and in another paralysis of the anal sphincter persisted for 10 days. Sixteen patients had urinary retention for more than 24 hours.

Comments

A number of advantages may be ascribed to the catheter method of continuous caudal anesthesia.

1. *Safety*.—A soft, flexible catheter is undeniably safer than a steel needle. Needle breakage is now rare, but there is always the possibility of a shift in position of the patient. Any such movement often dislodges an inlying needle, with the result that subsequent injections no longer reach the caudal canal. More dangerous, however, is the risk of piercing the dura or blood vessels. Once the catheter has been properly placed, it cannot be dislodged and subsequent injections can be made safely and effectively.

2. *Position of the Patient*.—Complete freedom of movement is permitted the patient. Descent of the fetal head often has been impeded by the lateral position necessitated by the needle method. The catheter allows the patient to remain on her back with safety. She may be transported to and from the delivery room without interrupting the anesthetic.

3. *Facility of Insertion*.—We have found that it actually is easier to manage the rigid 15 gauge needle than the malleable type. This is particularly true within the caudal canal, where the operator must be able to control the needle point.

4. *Obesity*.—Caudal anesthesia with the inlying needle method is often impossible in the obese patient. This is because the usual malleable needle is not long enough to penetrate the pad of fat over the sacrum and remain in the caudal canal. Moreover, the needle is readily dislodged by the motion of the fat itself. If the obesity does not prohibit locating the canal, a catheter may be inserted to the proper level and anchored securely in position.

Summary

1. A technique for the catheter method of continuous caudal anesthesia is described.

2. A series of 300 unselected cases is reported. There were 6, or 2 per cent, complete failures, and 23 patients (8 per cent), who required supplemental anesthesia.

3. There were no maternal deaths. Seven babies were lost, the deaths of none of these could be attributed to caudal anesthesia.

4. The catheter method possesses the advantages of increased safety, freedom of movement by the patient, and facility of insertion.

References

1. Manalan, S. A.: J. Indiana State M. A. 35: 564, 1942.
2. Adams, R. C., Lundy, J. S., and Seldon, T. H.: Proc. Staff Meet. Mayo Clinic 18: 97, 1943.
3. Idem: J. A. M. A. 122: 152, 1943.
4. Siever, J. M., and Mousel, L. H.: J. A. M. A. 122: 424, 1943.
5. Irving, F. R., Lippincott, C. A., and Meyer, F. C.: New York State J. Med. 43: 1023, 1943.
6. Irving, F. R.: J. A. M. A. 122: 1181, 1943.
7. McCormick, C. O., Huber, Carl P., Spahr, John F., and Gillespie, Chas. F.: AM. J. OBST. & GYNEC. 47: 297, 1944.

2398 SACRAMENTO STREET

SIMILARITY OF MOUTH AND VULVAR LESIONS

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THE purpose of this presentation is to point out a clinical correlation of lesions common to the mucosa of the mouth and to the mucosa of the vulva. A brief review of embryology will illustrate that there are structural anatomical similarities between the mouth and the vulva.

In the early embryo, the foregut and the hindgut end blindly. The pharyngeal membrane separates the stomodeum from the anterior end of the foregut; in the breech, the intestinal, urinary, and genital tracts open into a common space, the cloaca, which is separated from the outside by the cloacal membrane. The pharyngeal membrane is formed by fusion of the stomodeal ectoderm and foregut entoderm; the cloacal membrane consists of ectodermal cells and entoderm of the hindgut. Both of these membranes disappear in the early weeks of embryonic development.¹ The mouth is developed from the stomodeum and partly from the floor of the foregut. The vulva is of ectodermal origin and surrounds the exits of the urinary, vaginal, and rectal orifices. The salivary glands develop as buds from the epithelium of the mouth of the embryo between the fourth and ninth weeks. Salivary secretions are not fully established until the fourth month of infancy.² Bartholin's glands are developed by the third month and contain mucus by the fifth month of fetal life.³ Secretions from the parotid, submaxillary, sublingual, and labial glands of the mouth are alkaline. The mucoserous discharge from Bartholin's glands is also alkaline. Secretions from both the oral and vulvar glands are subject to control of the autonomic nervous system.

Sweat glands are of interest in that the vermilion borders of the lips and the labia minora are the only surface areas of the female body completely devoid of the small eccrine sweat glands.⁴ The large apocrine sweat glands, associated with hair follicles, are in abundance on the mons veneris, the labia majora, the perineum, and to a much lesser degree in the skin about the lips. Sebaceous glands normally open into hair follicles, but on the vermilion borders of the lips and on the hairless labia minora they open directly on the surface.

The vestibule of the mouth, that area between the teeth and gums and the lips and cheeks, and the vestibule of the vulva, the space between the labia minora, are quite similar with regard to temperature, degree of anoxia, and texture of the surrounding tissues. With nasal breathing, there is very little more oxygen in the mouth than is ordinarily present in the vulvovaginal area. The lips and the labia minora are particularly well supplied with nerves, blood, and lymph vessels.

Congenital abnormalities in the mouth are usually cleft or fusion defects while the most common anomalies of the female genitalia are hymenal or Müllerian duct deformities.

For satisfactory examination of either the vulva or mouth, it is important to have the patient in a proper position with adequate illumination and satisfactory instruments for visualization. For protection to himself and to his patient, the physician should wear rubber gloves for palpating lesions in the mouth or on the vulva. Regional lymph gland palpation is of distinct value in both areas.

Color of the Mucosa

With few exceptions, systemic factors influencing circulation to the mucosa of the mouth and vulvovaginal area cause similar color changes. Anoxia due to anesthesia, pulmonary or cardiac disease results in cyanosis of the vulvar and oral mucosa. Anemia causes pallor in both areas. Jaundice gives a yellowish color to the mucosa. Certain poisons such as carbon monoxide, sulfanilamide, and the aniline dyes change the color of the circulating blood by reducing oxyhemoglobin. Polycythemia results in a rich red discoloration of both the oral and vulvovaginal mucosa.

Changes in Menstruation, Pregnancy, and the Menopause

Of particular interest to the obstetrician and gynecologist are the mucosal changes found in the menstrual cycles, in pregnancy, and in the menopause. Systemic premenstrual vascular changes bring about submucosal engorgement and redness in the mouth. Premenstrual engorgement of the vulvar mucosa is usually a deeper, reddish blue. Premenstrual edema of the lips, face, and vulva occasionally occur. Cyclic endocrine changes influencing the oral mucosa may give rise to hyperemia and bleeding of the gingivae in association with menstruation. This condition is known as stomatitis dysmenorrhoeica.⁵

Oral changes associated with pregnancy are those of hypersecretion and tissue proliferation. Early in pregnancy salivary secretions are increased. Ptyalism is an annoying, contributory factor in the early vomiting of pregnancy. The gravid patient often experiences changes in taste perception and appreciation. A proliferative marginal gingivitis occasionally occurs in pregnancy. The overgrowth of the gum margins in stomatitis gravidarum may be extensive enough to cover the teeth. The micropathology of this pregnancy tumor is that of an angiomatous proliferation in fibrous tissue. The gingivae generally return to normal after delivery.⁶ Other benign tumors of the gums frequently enlarge during pregnancy. If these tumors are removed during gestation, the recurrence incidence is greater.⁷ Secretions from the genital glands are more profuse during pregnancy. Papillomas and condylomas recur more frequently when they are removed from the pregnant patient. The smooth tongue and the pale buccal mucosa of the last trimester of pregnancy are usually associated with hypochromic anemia. The vulvar mucosa of the gravid patient may be pale, but venous congestion of the vagina and cervix gives rise to blueness of that mucosa.

The atrophic menopausal changes in the mucosa of the mouth and vulva are quite similar. The menopause is accompanied by a decrease in salivation and in vaginal secretions. The mucosa becomes dry, glazed, and much less resistant to infection. Older women frequently complain of dryness and burning of the mouth and of irritation and itching of the vulva. Estrogenic therapy will give relief of symptoms from both areas. The estrogenic hormone increases cell activity and specialization. Resistance to mouth and vulvar infections is heightened by activation of the mucosa with estrogens.^{8,9} However, neither estrogenic nor vitamin therapy is indicated in the patient with definite kraurosis or leucoplakia of the vulva. These advanced premalignant skin changes require vulvectomy as the safest method of management.

Blood Dyscrasias

In severe relapses of pernicious anemia, bald atrophic tongue, ulceration of the lips and buccal mucosa, and superficial ulceration of the vulva occur along with hyperpigmentation of the surrounding skin. There is evidence to indicate that these mucosal changes are due to a combination of achlorhydria and vitamin B deficiency.^{10,11} In aplastic anemia and in leukemia, stomatitis and vulvitis are manifested by bleeding gum margins, ulceration of the oral and vulvar mucosa. Ulcerations in both areas are frequently infected with fusospirochetal organisms.

Local Infections

One of the most common surface infections of the oral and vulvovaginal mucosa is thrush, or moniliasis, due to the *Monilia albicans*. *Monilia* will not grow on healthy mucous membrane, but thrive on mucosa which is subjected to trauma or lowered resistance. Poorly nourished infants, diabetic women, and anemic pregnant patients are good candidates for moniliasis. In methods of resuscitation, it is well for the obstetrician not to traumatize the mouth of the infant with his gloved hand which has been contaminated by the vaginal discharges of the mother.

Diphtheria develops in an alkaline medium and in an abundance of air. The disease is characteristically one of the pharynx. However, oral and vulvovaginal diphtheria occasionally occur.

Tuberculous ulceration, present on the vulva or in the mouth, is usually found in the patient with far-advanced pulmonary or enteric tuberculosis.

Chancroid is a disease of the vulva which can be transplanted to the oral mucosa.

Gonorrheal stomatitis is rare; gonorrheal vulvovaginitis is the most common of venereal diseases.

Psoriasis, herpes simplex, lichen planus, and impetigo are local diseases, which may affect either the mouth or the vulva.

Skin irritation of the vulva and perineum secondary to a chronic, profuse alkaline cervical discharge compares with changes seen in lips

and chins which have been subjected to constant dribbling from the mouth.¹²

Vincent's fusospirillae are common secondary invaders of vulvar ulceration just as they are of lesions in the mouth.

Tumors

Benign and malignant tumors of connective tissue, blood and lymph vessels, and epidermis occur in the mouth and on the vulva. There is no definite relationship between the two except that syphilitic leucoplakia is quite common to both areas. Stokes' statement, "on finding leucoplakia, look backward toward syphilis and forward to cancer"¹³ can apply to both areas. Diffuse fibromatosis of the gingivae has the gross and microscopic characteristics of venereal condylomas.

Systemic Diseases

The most serious systemic disease common to the vulvar and oral mucosa is syphilis. Breaks in the mucosa are not necessary for inoculation with *Treponema pallidum*. The labia majora are second only to the cervix as the initial site of syphilis in the female.¹⁴ The lip is the most frequent extragenital area for chancre. The most open and infectious lesions of secondary syphilis, i.e., condylomata lata and mucous ulcers, are found on the vulva and in the mouth. Until secondarily infected, syphilis of the mucous membrane is fairly typical and usually painless. Macular and erosive syphilides are found on the mouth or labia minora; papular syphilis is common on the vulva, but rare in the mouth; ulcerative and sclerous syphilides occur in both areas. Hutchinsonian teeth and rhagades are evidence of congenital syphilis.

Diabetic stomatitis and vulvitis are quite similar. The mucosa membrane in both areas is dry, parched, and deep red in color. The patient complains of a burning sensation in the mouth and on the vulva.

In uremic stomatitis, the mouth changes are more profound than in the vulva. The tongue becomes dry, thick, and brown coated. The oral mucosa is inflamed and ulcerated. The gingivae bleed easily, and the uvula becomes swollen. The vulva frequently becomes edematous, reddened, and ulcerated. The discharges from the mouth and from the vagina have a uriniferous odor.

In recent years, physicians and nutritionists have made extensive studies in vitamin deficiency diseases. A scientific basis has been established for the reliance the old family physician placed on the tongue as an indicator of dehydration and malnutrition. Changes in the dorsum of the tongue, the buccal mucosa, and lips often reflect vitamin deficiencies secondary to gastroenteric and febrile diseases. Gynecologists have noted the effects of vitamin deficiencies on the mucocutaneous surfaces of the vulva.^{15, 16} B₂, or riboflavin, deficiency is manifested by a red, raw tongue, shiny, red mucosa of the lips and buccal surfaces, and an angular cheilitis.¹⁷ A similar shiny redness and rawness of the vulva occurs. A riboflavinosis favors the development of monilial infection.

Vitamin B₂ is specific therapy. The lesions will not respond to nicotinic acid alone. Pellagra, due to a deficiency in nicotinic acid and other factors of the B complex, produces soreness, redness, and ulceration of the tongue, gums, oral mucosa, and lips, vulvovaginitis, thickening and pigmentation of the skin. Pellagra favors secondary infection with Vincent's organisms.¹⁸ An adequate diet supplemented with nicotinic acid and brewers' yeast will initiate tissue repair of both the oral and vulvar lesions. With the widespread use of estrogens and with evidence that they stimulate tissue regeneration, it is of interest to note that Ashworth and Sutton found that "estrogens do not aid in the utilization of the vitamin B Complex."¹⁹ According to their evidence, estrogens given to individuals with subclinical vitamin B complex deficiencies caused the appearance of characteristic polyneuritis, pellagra, and cheilitis.

Conclusions

There is a structural embryologic, anatomic, and physiologic similarity between the mucosa of the mouth and vulva. Certain local and systemic infections influence both areas. The patient may complain of symptoms from only one area, when similar lesions can be found both on the vulva and in the mouth. The importance of a thorough examination of both areas is stressed. Women frequently consult the doctor early about mouth lesions, but they are somewhat reluctant to seek advice at the onset of genital symptoms.

References

1. Arey, L. B.: *Developmental Anatomy*, ed. 3, Philadelphia, 1937, W. B. Saunders Company, p. 170.
2. Prinz, Hermann, and Greenbaum, S. S.: *Diseases of the Mouth and Their Treatment*, Philadelphia, 1935, Lea and Febiger, p. 24.
3. Taussig, Frederick J.: *Diseases of the Vulva*, New York, 1926, D. Appleton and Company, p. 6.
4. Hunt, Elizabeth: *Diseases Affecting the Vulva*, St. Louis, 1940, The C. V. Mosby Company, p. 16.
5. Thoma, Kurt H.: *Oral Pathology*, St. Louis, 1941, The C. V. Mosby Company, p. 1206.
6. Thoma, Kurt H.: *Ibid.* p. 1060 and p. 1207.
7. Prinz, Hermann, and Greenbaum, S. S.: *Ibid.* p. 108.
8. Ziskin, D. E.: *J. Dent. Research* 16: 367, 1937.
9. Thoma, Kurt H.: *Oral Pathology*, St. Louis, 1941, The C. V. Mosby Co., p. 55.
10. Oatway, W. H., and Middleton, W. S.: *Arch. Int. Med.* 49: 860, 1932.
11. Hutter, A. M., Middleton, W. S., and Steenbock, H.: *J. A. M. A.* 101: 1305, 1933.
12. Hunt, Elizabeth: *Diseases Affecting the Vulva*, St. Louis, 1940, The C. V. Mosby Company, p. 59.
13. Stokes, John H.: *Modern Clinical Syphilology*, ed. 2, Philadelphia, 1934, W. B. Saunders Company, p. 830.
14. Davies, T. A.: *Primary Syphilis in the Female*, London, 1931, Oxford University Press, p. 10.
15. Dabney, M. Y.: *South. Surg.* 8: 232, 1939.
16. Hesseltine, H. C.: *AM. J. OBST. & GYN.* 42: 702, 1941.
17. Sydenstricker, V. P., Geeslin, L. E., Templeton, C. M., Weaver, J. W.: *J. A. M. A.* 113: 1697, 1939.
18. Spies, T. D., Vilter, R. W., and Ashe, W. F.: *J. A. M. A.* 113: 931, 1939.
19. Ashworth, J., and Sutton, D. C.: *Arch. Int. Med.* 69: 15, 1942.

FIVE HUNDRED CONSECUTIVE CESAREAN SECTION OPERATIONS*

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IN this report and analysis we have studied a group of 500 consecutive cesarean sections performed at Chicago Lying-in Hospital from March 1, 1938, to March 6, 1942. This series of cesarean sections constitutes a complementary third group of 500 cases operated upon consecutively in this institution from May, 1931, to March, 1942. The prior two groups totaling 1,000 cases were analyzed by Daily in 1939. Interest lies in comparison of results; hence, in summary, certain factors in statistical change will be noted.

From March 1, 1938, to March 6, 1942, there was a total of 11,281 deliveries at Lying-in Hospital, giving a section incidence of 4.43 per cent for this particular group and period.

Thirty-three operators were responsible for the surgery in the series. The departmental staff of Lying-in Hospital consisting of full-time members and residents handled 398 of the cases. The remaining 102 cases (20.4 per cent) were operated upon by members of the practicing courtesy staff. No one individual operated upon more than 13.8 per cent of the cases (69).

Types of Operative Procedure

455 Laparotrachelotomies	91.0%
205 Laparotrachelotomies with tubal ligation	41.0%
2 Classical with tubal ligation	
1 Laparotrachelotomy with cornual resection	
37 Cesarean hysterectomies	7.4%
4 Classical cesarean sections	0.8%
4 Vaginal cesarean sections	0.8%

First Section

306 Cesareans	61.2%
271 Laparotrachelotomies	
28 Cesarean hysterectomies	
3 Classical	
4 Vaginal	

Second Section

167 Cesareans	33.4%
159 Laparotrachelotomies	
7 Cesarean hysterectomies	
1 Classical	

Third Section

26 Cesareans	5.2%
24 Laparotrachelotomies	
2 Cesarean hysterectomies	

Fourth Section

1 Laparotrachelotomy	0.2%
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Maternal Mortality

There were two deaths in the series for a percentage of 0.4. One of these patients died of cerebral hemorrhage and/or eclampsia. The patient was considered a poor risk at the time of operation. No anesthetic was required. The other death resulted from hemorrhage and shock following cesarean section in a case of total placenta previa.

*Presented at a meeting of the Chicago Gynecological Society, April 21, 1944.

Fetal Mortality

There were 35 neonatal and 11 intrapartum deaths; giving a fetal mortality of 9.2 per cent for the 500 sections. In the neonatal group 22 of the cases were premature, 10 were previable (91.5 per cent). In the stillborn group, 4 cases were premature and 4 previable (72.7 per cent). In both the neonatal and intrapartum series, the antecedent maternal pathology was largely toxemia, abruptio placenta and placenta previa. It was noted as 10 cases of toxemia, 5 cases of abruptio placenta, and 9 cases of placenta previa in the neonatal deaths; and 2 cases of toxemia, 4 cases of abruptio placentae, and one of placenta previa in the intrapartum deaths.

Maternal Morbidity

The morbidity standard used has been that of the American Committee on Maternal Welfare. The mortality figure in the series was included in the morbidity evaluation. There were 155 febrile cases using this index (31 per cent): 70.9 per cent of the morbidity (110 cases) was genital in origin; 12.9 per cent (20 cases) resulted from urinary tract infections; and 3.8 per cent of the morbidity (6 cases) was attributed to respiratory tract infections. Transfusion reactions, thrombophlebitis and wound infections about equally accounted for 7.1 per cent of the morbidity (10 cases), and 9 other cases were, in total, responsible for the remaining 5.8 per cent of the morbidity with various diagnoses other than these listed.

Effect of Labor and Ruptured Membranes on Morbidity

We have been interested in this particular feature of this study not only because of its primary importance but, also, because of the stress laid on such morbidity findings in some of the contributory literature and in clinical consideration. For these reasons, we have analyzed the group in somewhat more detail than is usual.

In the 500 sections, 300 cases were neither in labor, nor had ruptured membranes (60.0 per cent). Eighty-six of these sections became febrile (28.6 per cent). Of the total number of sections, 164 (32.8 per cent) were in labor; 59 (35.9 per cent) of these were febrile. A total of 119 cases (23.8 per cent) had ruptured membranes and 42 of these were febrile (35.3 per cent). Thirty-six cases were not in labor and had ruptured membranes; 11 of these became febrile for a percentage of 30.5. Eighty-three cases both were in labor and had ruptured membranes (16.4 per cent); of this group 31 were febrile (37.3 per cent). With membranes unconsidered, 56 cases were in labor less than 12 hours, and 49 cases were in labor more than 12 hours and were afebrile. The morbid cases under the same conditions about balanced—31 and 28. In the instance of ruptured membranes for less and more than 12 hours, disregarding labor, the afebrile cases were noted as 45 and 32; the febrile cases 21 and 21. In the cases both in labor and with ruptured membranes for less and more than 12 hours, the febrile per-

centages of 32.2 and 46.1, respectively, gave an indication of the higher morbidity in such cases. Further, with only one exception, the morbid percentages throughout the group were noted to be higher where the element of time increased in relation to labor. Though the number of cases for comparison was small, it was likewise noted that morbidity increased by an approximate one-fourth when labor accompanied ruptured membranes, 37.3 per cent and 30.5 per cent, respectively. Moreover, it is significant that the febrile percentage of 28.6 noted in those cases operated upon under the conditions of intact membranes and no labor was within 1 per cent of the lowest morbidity evaluation found under any conditions.

Effect of Toxemia on Morbidity

Out of a total of 92 cases of toxemia, 46 cases were febrile (50 per cent). In the sections for abruptio placenta, toxemia being frequently a common factor, 5 cases out of 13 were morbid (38.5 per cent).

Effect of Secondary Section on Morbidity

Of the 271 laparotrachelotomy first section cases, 95 were morbid (35.1 per cent). Of the 159 second section cases, 40 were febrile (25.1 per cent). Out of the 24 cases of third section, 3 (12.6 per cent) were febrile. Thirteen of the 37 cesarean hysterectomies were morbid (35.1 per cent); 3 of the 4 vaginal sections were morbid (75 per cent); and one of the 4 classical sections was morbid (25 per cent). The decreasing morbidity noted in the second and third multiple section cases was due to the fact that they were usually elective; the conditions which contributed to morbidity at first section not being present on secondary section.

Indications for Cesarean

There was a total of 306 primary sections in the series (61.2 per cent). This is an inclusive figure comprising the total of laparotrachelotomies, cesarean hysterectomies, classical and vaginal sections.

Dystocia and Disproportion.—Cephalopelvic disproportion, 75; Contracted pelvis, 30; Fibroid uterus, 16; Prolonged labor with inertia, 9; Vaginal plastics, 9; Elderly primipara, 4; Stillbirth history, 4; Cervical dystocia, 3; Contraction ring, 2; Transverse, 2; Uterine anomalies, 2; Dystrophy-Dystocia Syndrome, 1; Brow, 1; Face, 1; Ovarian cyst blocking pelvis, 1.—160 cases (32.0 per cent).

Toxemias.—Pre-eclampsia, 37; Eclampsia, 8 (8.0 per cent); Hypertension, 22; Nephritis and Pyelitis, 13 (7.0 per cent). Total 75 cases (15.0 per cent).

Hemorrhage.—Placenta previa, 39; Abruptio placenta, 13; Ruptured uterus, 2.—54 cases (10.8 per cent).

Cardiac.—12 cases (2.4 per cent).

Other Indications for Primary Section.—Diabetes, 2; Pulmonary tuberculosis, 1; Premature rupture of membranes with intrauterine death of fetus, 1; Spastic paralysis, 1.—5 cases (1.0 per cent).

The predominating indication for operating the remaining 194 (38.8 per cent) cases was previous section. This was combined with a desire to sterilize in many instances; in others, the primary indication carried

over and enhanced the indication for secondary section. Cases of contracted pelvis, hypertensive vascular disease, nephritis, and certain chronic diseases are illustrative of continuing concomitant indications which reinforced the indication for secondary section. However, for the purpose of later comparison, when continuing, recurrent or variant pathology was noted as a distinct factor in the indication for secondary section, this indication was then considered as primary in analysis. Thus, in this group there were 113 cases (22.6 per cent) having disproportion and dystocia as an indication for repeat section, 17 cases of toxemia (3.4 per cent), five cases with vaginal hemorrhage (1 per cent), three cardiacs (0.6 per cent), and four cases of miscellaneous pathology (0.8 per cent). The remaining 52 cases (10.4 per cent) had no other significant noted indication for section save previous cesarean.

Previous Section and Sterilization

Of 167 cases having had 1 previous section, 113 were sterilized (67.7 per cent). Twenty-six cases had had two previous sections; all of these were sterilized (100 per cent). One case had a fourth section; this case was sterilized (100 per cent). Of the 271 primary laparotomies, 77 (28.4 per cent) were sterilized by tubal ligation (Madlener).

Stillbirths

There were 310 multiparas in the series (62 per cent). In 38 of these, there was a history of one or more stillbirths (12.2 per cent). The obstetric history in the majority of these cases rather closely followed the expected pattern, i.e., contracted pelvis, prolonged labor, toxemia, or one of the hemorrhagic accidents. This type of history frequently constituted an influencing factor in the indication for operation.

Period of Gestation

Two hundred and forty-eight cases (49.6 per cent) were 36 to 40 weeks; 103 cases (20.6 per cent) were 40 weeks; 79 cases (15.8 per cent) were 41 to 44 weeks; 69 cases (13.8 per cent) were less than 36 weeks; 1 case (0.2 per cent) was over 44 weeks.

The indications for interference in the 69 cases under 36 weeks were almost entirely abruptio placenta, placenta previa, or toxemia.

Anesthesia

Local alone—280 cases (58 per cent); local and cyclopropane—62 cases (12.4 per cent); local and ethylene—12 cases (2.4 per cent); local and ethylene and ether—3 cases (0.6 per cent); cyclopropane—110 cases (22 per cent); ethylene—8 cases (1.6 per cent); ethylene and ether—19 cases (3.8 per cent); ethylene and ether and cyclopropane—2 cases (0.4 per cent); cyclopropane and ether—2 cases (0.4 per cent); cyclopropane and ethylene—1 case (0.2 per cent); none—1 case (0.2 per cent).

A solution of one-half per cent novocain in local infiltration held predominant position as an anesthetic agent. As complementary anesthesia, cyclopropane was favored over ethylene or ether. Cyclopropane alone was used in over one-fifth of the cases, the indications usually being an uncontrollable or nervous patient, or necessity for rapid operation.

Summary

The maternal mortality in the first two series comprising 1,000 cases of cesarean section was 0.8 per cent. In the last 500 cases, it was 0.4 per cent, demonstrating a 50 per cent decrease. Maternal mortality for the 1,500 cases was 0.66 per cent. Four of the deaths in the first 1,000 cases resulted from infection of genital origin. No deaths in the last group were attributed to puerperal sepsis, as attested by autopsy.

The morbidity in the earlier series was 43.8 per cent. The morbidity in this latter group was 31 per cent. This was a decrease of 29 per cent in total morbidity in the last four years. The combined morbidity for the entire 1,500 cases was 39.5 per cent.

Fetal mortality was noted to be 6.7 per cent in the first 1,000 cases. In this latter series, it had risen to 9.2 per cent. Part of this rise in fetal mortality was due to a rise in the incidence of section in toxemias. In the first 1,000 cases, 12.3 per cent of the sections were performed with the indication toxemia and related conditions. In this latter group 18.4 per cent of section incidence was attributed to toxemia. The necessity for early interference in the fulminating toxemias increased fetal mortality.

The incidence of section in the earlier group was 5.5 per cent. The recent series showed a section incidence of 4.43 per cent; the incidence decreased approximately 20 per cent in comparison.

There was a variance in the relationship of indications for section between the first series and this latter. The greatest disparity was noted in three groups. Multiple sections increased from 27.9 per cent in the first series to 38.8 per cent in the latter. More section cases are returning for reoperation. Cardiac pathology as an indication for section was noted as 10.4 per cent in the first 1,000 sections. It was down to 3 per cent in this last study. Cesarean section incidence in heart disease is on the decrease for two reasons. Many of these cases where pregnancy is a distinct hazard are being interrupted early with sterilization, or with helpful contraceptive advice; and many others under careful medical observation and control are being carried to late viability or term with subsequent safe vaginal delivery.

Toxemia, as an indication for interference, accounted for 12.3 per cent of the sections in the earlier series: in the last 500 cases, this indication had risen to 18.4 per cent. This reflects the tendency to adopt an active obstetric attitude toward the problem of severe and unresponsive toxemia.

Conclusions

The maternal mortality and morbidity of cesarean section in Chicago Lying-in Hospital have shown a continuous decrease from 1931 to 1942. It is probably not yet irreducible.

Though the indications for cesarean section have become in the past decade probably somewhat more comprehensive, the incidence of cesarean section has decreased. Careful selection of cases has operated in favor of vaginal delivery, and primary elective section for the purpose of sterilization has, in the main, been supplanted by postpartum tubal ligation.

The low flap transperitoneal section is the operation of choice in this institution. General procedure and technique have not changed, but critical attention as to indication and time for interference has contributed to improve statistics.

I wish to express my appreciation to Dr. W. J. Dieckmann for his helpful criticism in the preparation of the manuscript.

Discussion

DR. PHILIP H. SMITH.—The members of our department at the Evanston Hospital have been pleased with our results in cesarean section. It is, therefore, satisfying when I note the close similarity between several of the important figures and percentages in Dr. Free's report and our own statistics.

In a fifteen-year period—1929 through 1943, we have delivered 13,575 women. The incidence of cesarean section in this group was 3.88 per cent, while Dr. Free reports 4.43 per cent incidence. We regularly do the low cervical operation, and during this period less than a dozen classical operations were done.

Our maternal mortality is 0.9 per cent as against 0.4 per cent for the recent Lying-in series. The deaths in our group have been due to pulmonary embolism, postoperative hemorrhage, peritonitis and toxemia with pneumonia.

Our fetal mortality of 9.3 per cent compares with Dr. Free's figure of 9.2 per cent. These percentages are almost three times that for the fetal mortality when patients are delivered otherwise. Dr. Free has made it clear, however, that toxemia and nonviable states in bleeding cases, largely account for this.

Our morbidity is 33 per cent, while in the report it was reported at 31 per cent. I believe this figure to be largely dependent upon the length of labor and whether or not the membranes are ruptured.

While recognizing the important place abdominal delivery holds, there can be no doubt it is often done too frequently, and when the proper conditions cannot be met. While it may often be the easiest way out of a difficulty, it is not necessarily the safest and best. A figure in the vicinity of four per cent seems to be a fair one. The men at the Lying-in have only slightly exceeded 4 per cent, which is a reduction from their earlier group in which the incidence was 5.5 per cent. Our incidence of 3.88 per cent, particularly pleases us.

We have found it necessary to do cesarean section for about the same indications, and in like order of frequency, namely, repeat cesarean, disproportion, toxemia, and hemorrhage, etc.

Ethylene anesthesia is chiefly used in our department; local anesthesia is used in cases of toxemia.

I should like to ask Dr. Free first, how often they allow a woman to go into labor, who has had a previous section? Lately, our policy has changed a bit regarding this. If the indication for which the first section was done, does not now prevail,

some of these patients can be delivered safely. Second, what does he mean by vaginal cesarean section at term?

DR. FRED O. PRIEST.—The incidence of sections at the Lying-in Hospital is somewhat higher than that at the Presbyterian Hospital: 4.43 per cent, while ours has been 1.57 per cent. Since 1939, however, our incidence has risen to 3.52 per cent. We attribute much of this increase to the fact that our outpatient department was discontinued in 1940, thereby decreasing our total number of deliveries, while we have continued to draw a considerable number of repeat sections from that group.

Dr. Free reports also a much higher proportion of low cervical sections than we can report. His report is of recent work, while our report goes back to 1930, and our present trend is more and more toward the low cervical operation. Furthermore, we have not classified a case as low cervical even though the incision was chiefly in the lower uterine segment, if the upper portion extended into the lower fundus and was not completely covered by the bladder flap of peritoneum in closing. We could decrease our classical percentage markedly if we called these *Low Fundal*.

I am impressed by the ability of the operators in this report to use the true low cervical technique in such a high percentage of repeat sections—even in the third and fourth sections. They report doing only four classical operations in 194 repeat sections. We have not been able to maintain such a percentage.

Both our maternal mortality and morbidity have been higher than that reported by Dr. Free. On the other hand, we have had only twenty fetal deaths (uncorrected) or 6.8 per cent, while he reports 9.2 per cent.

Our indications for cesarean section and percentage done for each indication correspond closely with those at the Lying-in, except that we have done fewer for cardiac reasons. We have done a comparable number of sterilizations on repeat sections, though a much lower percentage on primary sections.

At least 90 per cent of our operations have been done under ethylene and oxygen. Most of the remainder have been toxemia or cardiac patients and were done under local anesthesia. No patient has been sectioned for cardiac reasons since 1937.

DR. J. P. GREENHILL.—On the supposition that this paper was to contain statistics from the Lying-in Hospital, I jotted down some figures from a paper I wrote fifteen years ago. In 1929, I compiled all the cesarean sections performed at the old Chicago Lying-in Hospital from 1915 to 1929. In 1916, the incidence of cesarean operations was only 0.6 per cent. That figure steadily rose until 1929, when it was 3 per cent, five times as great within a period of fourteen years. The incidence cited by Dr. Free was 4.43 per cent and the incidence given by Dr. Smith for the Evanston Hospital was 3.7 per cent.

Now as to mortality, among the 874 cervical cesarean sections which I analyzed, the death rate was 1.26 per cent. This is practically identical with the Presbyterian Hospital figure but considerably higher than the Chicago Lying-in figure for the last 500 cases.

In my group the indication for cardiac disease was only 3.3 per cent, which was definitely lower than the figure Dr. Free quoted. Only 50 per cent of the patients in my series were in labor, whereas in Dr. Free's group 60 per cent were in labor.

Local anesthesia was used in 58 per cent in my series. In 1929, the last year of my series, 92 per cent of all cesarean sections were done under local infiltration anesthesia.

I compared the death rate after the local cervical cesarean section with that following the classical operation. In the fifteen-year period, practically all the operations were done by six attending men, but most of them were performed by Dr. DeLee. During this fifteen-year period, the death rate in the classical group was three times as high as the mortality for the cervical operation. There were 38 Porro operations without any mortality.

What about the terminology when part of the incision extends into the lower part of the corpus of the uterus? I agree with Dr. Priest that in doing an elective cesarean section, we often have to extend the incision into the upper portion of the uterus a centimeter or more. I still call this a cervical operation. I think we will have difficulty separating these cases from the ones done as typical cervical cesarean sections. In all of these cases, we have the decided advantage of being able to use the bladder peritoneum for complete covering of the uterine incision.

DR. WILLIAM J. DIECKMANN.—The statistics given by Dr. Free include all abdominal hysterotomies of fetuses weighing 400 grams or more. So far as I know, Eastman is the only investigator who has stated that the term cesarean section should be limited to fetuses weighing 1,500 grams or more. The maternal morbidity and mortality for fetuses weighing less than 1,500 grams and especially for those weighing less than 1,000 grams are less than for those weighing more than 2,500 grams.

Some obstetricians are of the opinion that if they have an absolute indication for a cesarean section and the patient dies from the infection, that they are not responsible for it. We believe that if an elective cesarean section is performed and the patient develops sepsis, that the doctor and hospital are responsible irrespective of the indication for the cesarean section. We believe that the maternal mortality from cesarean section should be less than 0.5 per cent.

I have collected almost 2,000 cesarean autopsies, and the principal causes of death were:

Infection and ileus	38 per cent
Embolism	7 per cent
Hemorrhage and shock	30 per cent
Toxemia	19 per cent
Pneumonia	4 per cent
Anesthesia	3 per cent

It is obvious that more than two-thirds of these deaths, that is, those due to infection and most of those due to hemorrhage and shock, as well as those due to anesthesia and a considerable portion of those due to toxemia, are preventable and should not have occurred.

Hospitals should keep a strict account of their results, but they should not refuse to perform operations because it may affect their statistics. For example, one of our cesarean deaths occurred in an eclamptic patient. It was the opinion of the obstetrician in charge, who had been treating the patient medically for almost 24 hours, that the patient was moribund. He felt that the patient should be given a chance of survival, which is occasionally dramatically associated with delivery. This could have been performed by insertion of a bag or by cesarean section. The latter operation was selected because it was felt that time was a factor and a live baby might be obtained. The baby did survive although the mother died from eclampsia and intracranial hemorrhage. Two babies were salvaged by cesarean section on patients with tuberculous meningitis. Obviously, the cesarean statistics were not helped by these cases.

DR. FREE (closing).—The question frequently comes up in relation to a patient who has had a section, then has an intervening labor without a section, and then is again pregnant, whether this patient should be submitted to another section. We have a very definite opinion that all these cases should be sectioned.

In response to the second question, the four cases of vaginal section were included for comparative study with the other 1,000 cases; vaginal hysterectomy was included in the earlier 1,000 cases, and to make our statistics comparable, we included these four vaginal sections. In two cases the fetuses were dead.

A STUDY OF MATERNAL MORBIDITY*

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ABOUT 50 per cent of the maternal deaths in the United States are due to infection. Hemorrhage can usually be prevented, and if it occurs, may be readily treated by packing the uterus, and by the use of blood and plasma. Most serious toxemias of pregnancy can be prevented by proper prenatal care, and eclampsia has become rather rare in well-managed obstetric clinics. During the past ten years, there has been a small reduction in the number of maternal deaths from infection; but puerperal sepsis still remains the leading cause of mortality.

The source of puerperal infection may be either endogenous or exogenous. The former is not entirely preventable, but the attending physician can reduce this hazard by bringing his patient to term in the best possible physical condition. It has been shown that the removal of foci of infection will reduce morbidity. The prevention of anemia in the latter weeks of pregnancy is very important.

Bickerstaff¹ at Johns Hopkins recorded the hemoglobin levels of a large group of patients during the last four weeks of pregnancy. He found a marked decline in the incidence of febrility with increasing values of hemoglobin at this stage of pregnancy. During the last few weeks of pregnancy, nothing should be done to disturb the normal vaginal flora, and nothing should enter the vagina. It has been demonstrated that virulent bacteria are seldom found in the vagina or cervix unless they are introduced there.

In this connection Conti² demonstrated that a cervix with an erosion has no more organisms than a normal one, and that the morbidity is no higher in patients with erosions. He also demonstrated that the number of streptococci and the respiratory group of bacteria were both increased in cervical cultures during the months when respiratory infections are common.

Exogenous infection may be made less frequent by the use of careful aseptic and antiseptic technique, by the wearing of masks over the nose and mouth, by careful preparation of the patient and by avoiding contacts with attendants who may be carriers of virulent bacteria.

Hemolytic streptococci are the organisms responsible for most of the serious puerperal infections, and they are usually transmitted to the patient from the outside.

In the serious epidemic of deaths³ from puerperal sepsis at the Sloane Hospital in 1927, it was found that 20 per cent of the nurses, 8 per cent of the doctors, 25 per cent of the students and 8 per cent of the patients had positive cultures of virulent streptococci in their noses and throats. It was also discovered that there was an unusually large number of respiratory infections throughout that part of the country at the time, and that other hospitals reported a higher incidence of puerperal sepsis than was normal.

The use of vaginal instillations of various antiseptics during labor has apparently been a valuable addition to the technique of some institutions.

*Presented at a meeting of the Chicago Gynecological Society, April 21, 1944.

Mayes⁴ reported no maternal deaths in the last 11,000 vaginal deliveries and only one in the last 24,000, since they have used this procedure. The gross morbidity was 7.8 per cent and the corrected morbidity was 3.3 per cent. The gross figure had been 14 per cent before the use of mercurochrome instillations was begun.

In a survey he found that 517 out of 848 Diplomates of the American Board of Obstetrics and Gynecology use vaginal instillations during labor. In his survey of hospitals, 95,890 patients were delivered with only 12 deaths from sepsis as compared with 6 deaths in 13,424 deliveries where this procedure was not used.

Brown⁶ reported no maternal deaths from sepsis in patients having cesarean sections, since he has used vaginal instillations. In a study of cervical cultures, he found growths of bacteria in only 4 per cent when using this technique as compared to 44 per cent when it is not used.

I wish to present some statistics from the Evanston Hospital, covering a period of three years, from 1941 to 1944. There has been no important change in the technique used in the labor and delivery rooms for many years. We have not used routine vaginal instillations of antiseptics. It was used by one members of the staff but was later discontinued as there was no appreciable difference in his results. We insist that all attendants cover their noses and mouths, not only in the birth rooms but also on the maternity floor, when examining postpartum patients.

On admission to the labor rooms, patients are shaved and given enemas unless labor is too far advanced. Rectal examinations are used to determine the progress of labor except when an occasional vaginal examination is needed. When this, or any other vaginal manipulation is used, such as rupture of the membranes, the skin around the vulva is painted with an antiseptic solution and mercurochrome is instilled in the vagina with a syringe just before the examination is made. At the time of delivery, the skin is first cleaned with soap and then painted with an antiseptic before the patient is draped. We do not consider the skin as sterile, and maintain a "Hands Off" policy as much as possible.

Ergotrate is given intravenously at the end of the second stage by part of the staff, and intravenously at the end of the third stage of labor by others. It is not used routinely during the puerperium.

Although the maternity department is not housed in a separate building, it is isolated from the rest of the hospital, and the attendants do not have contact with other types of patients.

Almost all of our patients are under our control during the prenatal period and they are from a class which is well nourished, and they have whatever advantages a high economic standard may bring.

During this three-year period, there were 3,457 patients delivered in the hospital. Of these, 176 or 5.09 per cent developed a febrile morbidity. Removing those in whom the fever did not arise from the genital tract, the corrected figure is 3.64 per cent. There was one death in this group; this patient had a severe eclampsia. Postmortem examination showed terminal bronchopneumonia, necrosis of the liver and toxic nephrosis. Comparative statistics from different hospitals are difficult to correlate, as a different standard may be used. Morbidity rates from 6.5 per cent to 25 per cent have been published; a general average being about 10 per cent.

Our basis for morbidity is a temperature of 100.4° F. on any two days after the day of delivery. Temperatures are taken only twice daily unless there is fever. When fever appears, the temperature is taken every four hours. Many patients in this corrected group who had only two days of fever probably had fever from a source outside the genital tract, but unless a definite diagnosis was made they were all put in the puerperal sepsis group.

The number of days of febrility is important in studying maternal morbidity. A fever lasting two or three days is of little consequence and has little effect on the patient's convalescence; whereas, a fever lasting many days means a more serious infection which has probably spread beyond the uterus.

For detailed analysis of these patients I have eliminated those whose fever arose from outside the genital tract, because my object is to try to determine what obstetric procedures or complications cause puerperal sepsis.

This group of 124 patients had an average of 3.7 days with morbid temperatures. There were 52 who had a fever for 2 days, and 32 with fever for three days. Table I shows the total number of days morbidity.

TABLE I. DAYS OF MORBIDITY

Days	2	3	4	5	6	7	8	9	13	14	27
Patients	52	32	13	11	4	4	3	1	1	2	1
124 patients—Average days morbidity—3.7											

The average age of the women in this report was 28 years. About one-half of them were over 30. This corresponds with other reported statistics which show a lower morbidity up to age 30, with a rise above this age. This can be explained by a higher incidence of complications of pregnancy and labor in the older group.

The morbidity declines with advancing parity until a very high parity is reached; this also is caused by a larger number of complications encountered in primipara and again with high parity. Of the patients in this group, about 68 per cent were primiparas, whereas in the total number of patients delivered during the three years about 35 per cent were multiparas.

The average estimated blood loss was 230 cubic centimeters. This appears to be within normal limits, and as we had only four patients with a loss of over 500 cubic centimeters. I believe hemorrhage played a very small part in our morbidity. It has been shown that when blood loss is over 600 c.c., fever appears two to ten times as often.

The average length of labor was 12 hours and ten minutes, which is below average. The average length of labor of the patients with more serious and prolonged morbidity is greater than that of the entire group. This corresponds with the general impression that morbidity increases with the length of labor.

Pre-eclampsia occurred in 15 per cent of our morbid cases. This is about 6 per cent above average figures for the frequency of this complication and suggests that toxemias predispose to infection.

The various types of delivery showing the percentage of morbidity are shown in Table II. As might be expected, the more extensive operations carried with them the highest morbidity. This rate increases directly as the operation nears the uterus. Cesarean sections,

TABLE II. RELATION OF MORBIDITY TO OPERATIONS

	TOTAL CASES	MORBIDITY	
		CASES	PER CENT
Low cervical cesarean section	120	21	17.50
Classical cesarean section	3	2	66.60
Manual rotation	181	11	6.07
Midforceps	86	3	3.48
Low forceps	1,899	57	3.00
Breech extraction	105	4	3.80
Craniotomy	1	1	100.00
Version and extraction	13	0	0.00
Packing of uterus	38	14	36.84
Manual removal of placenta	46	4	9.09
Artificial rupture of membrane for induction	433	10	1.76
Loosening of membrane for induction	36	5	13.88
Cervical repair	194	11	5.67
Total operative	2,226	106	4.76
Spontaneous	1,253	25	3.19

packing the uterus and manual removal of the placenta, carried the highest morbidity rates.

The morbidity in the cases delivered operatively was 4.76 per cent. If the low forceps deliveries are removed from this group, the morbidity for the more difficult operations is 14.98 per cent. The figure of 3 per cent for low forceps compares very favorably with that for spontaneous delivery, which was 3.19 per cent.

Of the patients who had episiotomies or tears, 6.8 per cent had morbid temperatures. In only three of these was any infection of the repair discovered. The patients who had tears or episiotomies and no other operations or complications had only about 1 per cent morbidity, showing that this operation carries a very low morbidity.

In the total series of 3,457 patients, artificial rupture of the membranes for induction of labor was done 433 times or in 12.5 per cent. Loosening of the membranes for induction was done only 36 times. Also the membranes were ruptured after labor was in progress 136 times. This was done to stimulate labors which were not progressing, or just before delivery to remove a membrane which was retarding labor.

In the group of patients who were induced by rupturing of the membranes only 10 or 1.76 per cent developed puerperal infection. Of the patients who had the membranes loosened, 5 or 13.88 per cent developed puerperal sepsis. The insertion of a small sterile instrument into an open cervix is less likely to carry infection up from the lower genital tract than is the insertion of a finger, which is then smeared over the inner surface of the lower uterine segment. In a large portion of our cases, the perforator is passed into the cervix under the guidance of a finger in the rectum.

The frequency of induction of labor by this method may seem rather high but it is done only when the cervix is effaced and partly dilated, and the presenting part has entered the pelvis. As the figures show, it does not increase morbidity and we have had no increase in fetal mortality as a result of the procedure.

In Table III, the percentage of morbidity is shown by months. In general, it shows no regular seasonal variation. However, months when respiratory infections are common more often show a higher febrile morbidity. This has been borne out by others, such as Watson, at the Sloane Hospital.

TABLE III. SEASONAL VARIATION OF MORBIDITY

JAN.	FEB.	MAR.	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
5.07	7.87	7.53	3.80	2.95	2.83	5.01	5.32	7.09	4.79	4.14	4.79

The incidence of morbidity in the patients cared for by individual members of the staff was studied. No notable difference was found.

The prevention of puerperal sepsis is chiefly the responsibility of the physician. Certainly, a large majority of these infections are preventable. Most modern and well-managed obstetric clinics have reduced their morbidity, but there is still room for improvement. Patients are safer in hospitals than at home. At Johns Hopkins, the morbidity for women delivered at home was twice that of hospital patients. In the United States only 15 per cent of fatal puerperal infections developed in the hospitals.

The care of the patient in labor is probably the most important factor in lowering morbidity. Attention to details in aseptic and antiseptic technique is most essential and must be followed, not only in the delivery room but until the patient leaves the hospital. Various additions to the usual technique, such as vaginal instillations, are no doubt of value as has been shown by several authors, but they are not essential to good results.

It has been clearly demonstrated many times that major obstetric operations carry a higher morbidity. The unnecessary use of these procedures is to be condemned. Trauma in any form definitely increases the likelihood of infection.

The proper use of sedatives and the administration of nourishment during long labors will do much to lessen the exhaustion of the patients, and help bring them to delivery in the best possible general condition.

It has been suggested that when a uterus must be packed, the gauze should be impregnated with sulfanilamide; this supposedly acts as a prophylactic due to its bacteriostatic action. We have had no experience with this technique, but do use 0.5 per cent cresol gauze.

The value of the routine use of ergot in the puerperium to lower morbidity is not universally accepted. It has been argued that it may cause the spread of infection originally confined to the uterus by stimulating strong contractions. Others contend that keeping the uterus well contracted limits the spread of infection.

Since the introduction of the sulfonamides, the fear of puerperal infection has been somewhat lessened, and with good reason. The prompt and judicious administration of these drugs, when indicated, is of tremendous value.

At the onset of fever, cultures from the upper vagina or cervix should be made and examined within 24 hours, so that proper therapy may be used. Sulfanilamide is most effective against hemolytic streptococci, and sulfathiazole or sulfadiazine are best used for other types of infections. Supportive treatment with blood transfusions, proper diet and any measure which may improve the patient's general condition, must not be overlooked.

While all the methods of antisepsis and treatment of infection mentioned above have done much to lower maternal morbidity and mortality, proper prenatal care and skillful handling of the woman in labor are of prime importance. Too much reliance on drugs and antiseptics breeds contempt for careful obstetric technique and sound management of the patient in labor.

Summary

1. Infection is still the leading cause of maternal deaths in the United States.

2. The source of puerperal infection may be either endogenous or exogenous.

3. Much can be done to lower the incidence of puerperal sepsis by proper preparation of the patient in labor, and by the careful handling of her labor.

4. Three thousand, four hundred and fifty-seven patients were delivered at the Evanston Hospital from 1941 to 1944. The gross maternal morbidity was 5.09 per cent and the corrected rate was 3.64 per cent.

5. A summary of the routine used in the maternity department of the Evanston Hospital is presented.

6. The patients with puerperal sepsis are analyzed in detail. Those who had undergone major obstetric operations carried the highest morbidity rates. Those who were delivered with low forceps had a lower morbidity rate than the patients who were delivered spontaneously.

7. Artificial rupture of the membranes for the induction of labor caused no increase in febrility.

8. There was very little seasonal variation in the morbidity rate except for some increase during the months when upper respiratory infections were more common.

9. The prevention of puerperal sepsis is chiefly the responsibility of the attending physician.

10. The more recent additions to the treatment of puerperal sepsis are briefly discussed.

References

1. Bickerstaff, H. S.: *AM. J. OBST. & GYNEC.* 43: 997-1006, 1942.
2. Conti, E. A.: *Surg., Gynec. & Obst.* 73: 367, 1941.
3. Watson, B. P.: *AM. J. OBST. & GYNEC.* 16: 167, 1928.
4. Mayes, H. W.: *West. J. Surg.* 55: 201-209, 1943.
5. Mayes, H. W.: *New York State J. Med.* 43: 16, 1943.
6. Brown, T. K.: *Am. J. Surg.* 48: 164, 1940.

Discussion

DR. IRVING F. STEIN.—As Dr. Cummings has said, the last decade has shown little improvement in the mortality from sepsis, which is still the leading cause of maternal deaths. All of the efforts made to improve delivery technique have failed to provide an adequate prophylaxis.

Every attempt should be made to exclude carriers of virulent streptococci from birth room and nursery and routine examination for carriers should be made, as some of the most highly fatal epidemics have been traced to these sources. However, the parturient herself may enter the delivery room having an acute upper respiratory infection, thus presenting a potential menace to the maternity service as a whole.

The use of antiseptics in the birth canal has doubtlessly reduced morbidity in some clinics. However, Dr. Cummings reports a morbidity of 3.65 per cent among 3,457 patients in three years at the Evanston Hospital where this technique was not used as compared with 3.3 per cent reported by Mayes. Obviously, other factors are prominently involved. At Michael Reese Hospital, we found no essential difference in morbidity when using various antiseptic techniques such as tr. iodine, mercurochrome, tr. metaphen than when green soap and sterile water were

employed, so for several years we have completely abandoned the routine use of antiseptic preparations. Only sterile water is used during delivery. In two years we had 4,309 deliveries with a morbidity in 139 patients or 3.12 per cent.

The author's report of 10 of 433 who developed sepsis after puncture for induction, and 5 of 36 who were septic after loosening of membranes should be noted. Only green soap and sterile water are used in preparation for puncturing the membranes at Michael Reese Hospital. I personally do not subscribe to the routine rupture of membranes for the induction of labor, and, in fact, rarely induce labor at all. There are some obstetricians who do practice this procedure, however, with reported good results. For the simple puncture of membranes, I wish again to recommend the simple "midwife's fingernail" which I presented to this Society in 1935, and which we have used with great satisfaction for ten years. The use of the finger in the rectum as a guide for a vaginal operation, be it merely puncture of membranes, seems to me to be a reversion to the practice of former times when the doctor was not permitted to view the genitals but was required to examine women sight unseen.

Responsibility for the prevention of infection, insofar as is possible, rests unequivocally with the physician, and to this end, attention to careful aseptic delivery room technique is most important. In addition to the usually accepted measures, should we not consider the value of the sulfa drugs used on uterine packs, and in the uterine cavity and the peritoneal cavity during cesarean section as additional prophylaxis? In gynecologic operative work, we have used sulfathiazole gauze as drains with satisfactory results and this might well be adapted to obstetric operative technique.

The advent of sulfa therapy and the prospects of even greater and more spectacular cures from penicillin, gramicidin and perhaps as yet undiscovered preparations bid fair to decrease greatly the mortality and morbidity in obstetrics during the next decade. As Dr. Cummings warns, however, we must not allow careless habits to creep into the delivery room because of the curative value of sulfa drugs.

DR. J. E. FITZGERALD.—So-called maternal morbidity varies from the low figure noted by the author to upward of 20 per cent. This variation is due less to the difference in sick postpartum patients in good maternity services than to the frequency with which temperatures are recorded and to the type of cases corrected out from the gross number of febrile patients. I suspect that Dr. Cummings would have found more febrile reactions if temperatures had been recorded oftener than twice daily. We can, however, all agree on the main point of his essay, namely, that postpartum fever is more common after long and complicated labors, and in patients who are physically below par when they go into labor.

Maternal morbidity is an ugly term to describe a perfectly well patient who has two temperature readings of 100.4° F. in ten days. It is misleading to the public and the profession alike, because morbidity is by common usage associated with forms of illness more serious than the vast majority of these patients present.

The importance of an afebrile postpartum period and the reduction of true postpartum sepsis are not to be underestimated, but I believe we would get a better general picture of the postpartum period and more accurate statistics of postpartum fever if we could replace the term maternal morbidity by one more accurate and less ominous.

DR. CHARLES NEWBERGER.—During the year 1943, in hospitals of the state of Illinois, 285 mothers died, a mortality rate of 2.1 per 1,000 births.

The definition of the term morbidity is a temperature of 100.4° F. on any two occasions, excluding the first twenty-four hours, provided the temperature is taken

four times daily. This last-mentioned requirement must be observed. Many hospitals failed in giving adequate consideration to this matter. There were instances of hospitals reporting over 1,000 births with no maternal morbidity. One Chicago hospital reported 210 births in one month with no morbidity, but also indicated a maternal death from puerperal sepsis.

My remarks are intended to be a plea to physicians to see that the records are properly kept. Patients with toxemia or with hemorrhage are more apt to be reported as such than the patient who has temperature post partum. In an institution like the Evanston Hospital, I presume these records are kept more accurately and the results mean something, but in the average hospital that is not true.

In reply to the point that Dr. Cummings made about sepsis taking first rank in maternal mortality, I would like to point out that the survey made for 1943, of all obstetric deaths in Illinois showed that toxemia was responsible for 31.2 per cent, hemorrhage for 14.2 per cent and infection was the assigned cause in 12.6 per cent.

DR. W. C. DANFORTH.—The morbidity reported from the Evanston Hospital we thought might be questioned as being rather lower than it should be. I was interested to see, however, in a report that I received from Springfield the other day, that hospitals in this state with 1,000 or more births per year have a comparable morbidity. Hospitals that have that many births are the better run institutions, so that I think our morbidity is not out of line.

There has been a good deal of discussion about vaginal antiseptics and I very definitely feel that these are of little use. I think even that the use of antiseptics is contraindicated. The chief thing to do with the vagina of a pregnant woman, or a woman in labor is to leave it alone. Our technique, except for one short period when a few attempts were made to compare some of the different antiseptics, has been to use none. The use of an antiseptic solution on the skin I feel is more of a gesture than anything else. Thorough cleansing with soap and water is all we need.

As to puncture of the membranes for the induction of labor, I have never agreed that rupture of the membranes with an undilated cervix is a correct procedure, so rupture of the membranes with us has been confined to women with effacement and some opening of the cervix. We merely rupture the membranes by some simple means without any dilatation of the cervical canal. When one induces labor by introducing the finger in the cervix and swinging it around rupturing the membranes, it seems the danger of infection is greater. The flow of fluid afterward has some value in doing away with any introduction of infection. When we wish to rupture the membranes when there is 5 or 6 cm. dilatation, we do it by the use of a long narrow perforator.

DR. CUMMINGS (closing).—As Dr. Fitzgerald mentioned, taking temperatures only twice daily means we no doubt miss a certain number of infections, but I do not suppose we miss any that are serious. If the patient does develop a fever, we take the temperature every four hours. It was shown that most of the infections that developed had at least two or three days of fever.

Maternal morbidity figures as well as other statistics are hard to compare because hospitals use different standards. When we study the statistics from the State of Illinois, we find the morbidity rate is higher than ours, but apparently the Illinois figures are better than the country as a whole.

HIRSUTISM IN PREGNANCY

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A CONDITION commonly confronting the physician is that of excessive facial hair growth. Hirsute women often consider themselves ostracized not only by society, but by their husbands and families as well. Psychoneuroses may be precipitated or aggravated by this condition, yet few patients leave the gynecologist with their affliction relieved.

Multiple factors no doubt operate to produce this condition, yet investigation has proceeded largely along endocrine lines because certain hormonal abnormalities are commonly associated with hirsutism. Probably the commonest type of hirsute problem is the woman who develops facial hair growth at or after the menopause. The menarche may herald its onset. Amenorrhea often precedes or accompanies the onset of varying degrees of hirsutism. The administration of large doses of male sex hormones will produce this condition. Cushing's syndrome, a clinical term applied to cases with adrenal cortical hyperplasia, adrenal cortical tumors or thymus tumors is usually accompanied by excessive hair growth. Cushing's disease refers to a similar clinical picture, which has as its probable origin a basophilic adenoma of the pituitary. When the pathology can be recognized and corrected, improvement is to be expected. In the largest group of hirsutes, however, the cause cannot be found and the patient is finally referred to the dermatologist for depilatory treatment.

The condition to be discussed in this paper is not often of sufficient degree to cause concern either to patient or physician. This is evidenced by the paucity of reports in the literature.

While a number of authors¹⁻⁴ state that hirsutism commonly occurs in pregnancy, to this writer's knowledge, there are only five case reports in the literature. Slocum⁵ reported a patient who with each of three successive pregnancies developed marked facial hair growth. This fell out each time four to six months post partum. Hegar⁶ mentioned a case, but did not state whether the hair dropped out post partum. Hertzel⁷ and Jellinghaus⁸ had similar cases. McCarthy⁹ had a 36-year-old woman who developed this condition with each of three pregnancies. She noted a marked diminution in excess hair five weeks post partum.

Other authors have found a tendency toward alopecia during pregnancy or the puerperium. Ochs¹⁰ had a patient who with each of two pregnancies developed alopecia areata, only to regain her hair one month post partum each time. Becket¹¹ noted alopecia totalis following pregnancy in a 33-year-old woman. He makes no mention of the hair growing back.

Trotter¹² found no difference in rate of hair growth in seven women studied during pregnancy.

In experimental animals similar conflicting findings have been observed. Halban¹³ shaved the abdomens of pregnant and nonpregnant rabbits and found that hair growth was well established in the pregnant

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animals in four to five days, while in the nonpregnant one to two weeks was required. Dawson¹⁴ noted a definite decrease in the rate of hair growth during pregnancy in the guinea pig.

It appears, then, that in some species hair growth seems to be stimulated by pregnancy, while in others it is depressed. Human beings apparently may show stimulation, depression or no change in rate of hair growth during pregnancy.

Report of Cases

CASE 1.—(The author is grateful to Dr. A. Dale Kirk, Flint, Mich., for permission to report this case.)¹⁵



Fig. 1.

R. P., a 27-year-old primigravida, reported first for prenatal care July 3, 1936. Her last menstrual period had been May 29, 1936. On August 10, she reported excessive growth of hair on face, arms and legs and over her back. The growth was especially heavy on the sides of the face and under the ears where it appeared in small whorls. (Fig. 1.)

Menstrual history was normal. The patient had been known to have a low blood pressure for a number of years, and three years before, her basal metabolic rate had been low.

Physical examination was essentially negative save for the pregnancy and the hirsutism.

Basal metabolic rate was checked and found to be -11. Scout film of the abdomen failed to disclose any shadows suggesting adrenal tumors.

Roentgenogram of the sella turcica was found to be normal. Her eye grounds showed no abnormal findings.

The hair continued to grow throughout the pregnancy. On March 12, 1937, she spontaneously delivered a normal male infant.

About eight weeks post partum, she had a menstrual period. Shortly thereafter while taking a bath, she noted that on rubbing the skin surface with a rough turkish towel the hair could be rubbed off. She completed the hair removal that afternoon and her hirsutism disappeared. (Fig. 2.)

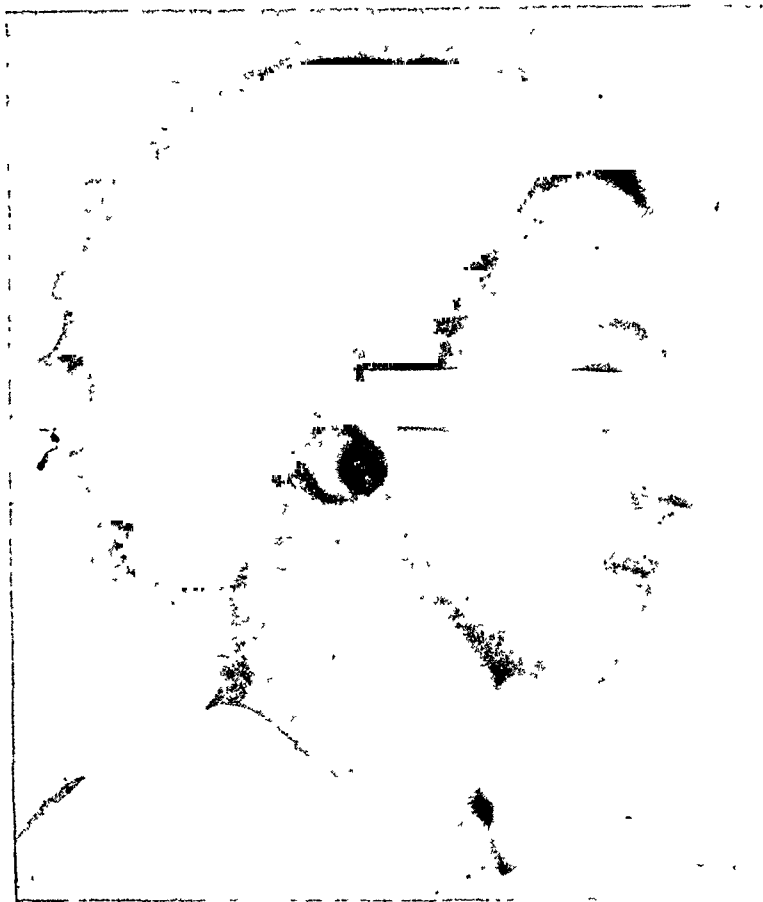


Fig. 2.

One and one-half years later, she repeated precisely the same performance. The patient has been seen on numerous occasions since then, and she is free from excess hair and there are no masculine characteristics.

CASE 2.—N.K., a 28-year-old primigravida, was first seen in the Department of Obstetrics and Gynecology of the University of Michigan Hospital in February, 1943. She stated that her last menstrual period was November 8, 1942, and that at about Christmas time she noted the rapid appearance of soft, luxuriant hair growth over the entire body, mostly on the face. (Fig. 3.)

Menstrual history had been perfectly normal. Neither she nor any of her relations had noted deepening of the voice or change in body habitus. Past medical history was noncontributory. No one in her family had suffered from a like condition.

Physical examination showed a normally developed woman with no masculinizing features other than the facial hirsutism, largely confined to the eyebrows and cheeks. A slight, but definite increase in growth had been noted on the upper lip and chin by the patient. There was also generalized hirsutism, but being blond it was not photogenic. One interesting feature is that the normal female pubic hair distribution remained unchanged. No purplish striae were noted. No abdominal tumors were palpable other than an apparently normal pregnant uterus. Pelvic examination was compatible with a three months' pregnancy. A sense of resistance was felt in the left adnexa. No hypertrophy of the clitoris was noted.

None of the roentgenograms showed osteoporosis. Scout film of the abdomen showed no abnormal calcification, nor any tumor masses in the upper abdomen. Chest and skull films were negative.



Fig. 3.

Blood pressure ranged from 130/85 to 140/88, hemoglobin from 56 per cent to 70 per cent and W.B.C. from 4,250 to 16,540. The only red cell count during the pregnancy was 2,850,000, taken when the hemoglobin was 56 per cent.

Urinary estrogens of 2.5 mg./24 hours were compatible with four months of pregnancy. The 17-ketosteroid levels of 12.0 and 8.2 mg./24 hours were definitely higher than our normal pregnancy range of 3 to 6.5 mg./24 hours. Aschheim-Zondek tests were positive with undiluted urine but negative with dilutions of 1:50 and 1:100.

Salt and water balance tests were considered as a means of estimating the degree of adrenal cortical activity. Due to the fact that salt and water balance in normal pregnancy is disturbed, it was felt that interpretation of such tests would be both difficult and unreliable in this case at the present state of our knowledge.

Perirenal air injection of the renal capsule to outline the adrenals was not attempted because of the very real risk in our experience of air emboli.

Finally, as a diagnostic measure, exploratory laparotomy was performed. This was elected for the following reasons: (1) The essentially negative physical findings save for the hirsutism and the resistance in the left adnexal region. (2) The elevated 17-ketosteroid levels suggested possible adrenal or ovarian pathology. (3) The feeling that if a possible hair growth producing tumor were allowed to grow unchecked, irreparable damage might result. (4) It was felt that if on exploratory laparotomy no tumor was found, the family could be dissuaded from considering termination of the pregnancy.

At the time of exploratory laparotomy, the uterus was the size of a four and one-half months' pregnancy. Several implants on otherwise healthy appearing ovaries were interpreted both grossly and microscopically as decidual implants. The adrenal glands were palpably normal both in size and consistency. The pregnancy was allowed to progress to a normal termination. The patient delivered a 7 $\frac{1}{4}$ -pound female infant on August 19, 1943. The infant has been followed regularly and is normal in every respect.



Fig. 4.

During the puerperium, the patient was followed closely and by November, 1943, the hair had definitely decreased. By January, 1944, all abnormal hair growth on the face and body had disappeared. (Fig. 4.) On November 2, 1943, the 17-ketosteroids were 3.4 mg./24 hours. The normal nonpregnant range in our series is 1.5 to 8.5 with an average of 5.3 mg./24 hours.

Discussion

In the differential diagnosis of this condition, we considered the causes of Cushing's syndrome, arrhenoblastoma, teratoma of the ovary,

an abnormally functioning placenta, and some abnormality of the fetus. The influence of the generalized hyperemia associated with pregnancy on the hair follicles of a susceptible individual was also considered as a possible cause. Our investigations failed to substantiate any of these possibilities. There are no published endocrine studies on this type of patient to the author's knowledge. The consensus of opinion among those who have studied these cases is that the hirsutism had its origin in the maternal adrenal cortex.

What evidence do we have for this belief? (1) The suggestively high 17-ketosteroid levels during pregnancy and the normal postpartum level in Case 2. These substances known to be associated with hair growth are normally formed in the adrenal cortex rather than the ovaries since castration does not alter the levels while adrenal atrophy as in Addison's disease causes a marked decrease. (2) Ovarian inspection and biopsy failed to reveal any possible etiology. (3) In experimental animals, the adrenal cortex is stimulated to increased size presumably by high levels of the hormones of pregnancy. This has also been demonstrated by administration of large doses of estrogens.

Certain questions must be answered before we can settle on the maternal adrenal cortex as the responsible factor. (1) Can the placenta, known to produce the steroid hormones, estrogens and progesterone, also under certain conditions elaborate a hair growth producing 17-ketosteroid? (2) Does inspection, palpation and random biopsy rule out the ovaries as etiologic factors? (3) Can some fetal factor influence maternal hair growth? (4) Are hair follicles in the susceptible individual stimulated to growth by the hyperemia of pregnancy?

Conclusions

Hirsutism of marked degree is rare during pregnancy. These cases should be studied thoroughly to rule out possible concomitant hair growth producing neoplasms. In the absence of definitely demonstrable neoplasms by clinical, laboratory or x-ray studies exploratory laparotomy offers little. The patient should be assured that the hirsutism will in all likelihood disappear post partum, but will probably return with subsequent pregnancies. There is no indication here for the termination of pregnancy.

References

1. Halban, J.: *Wien. klin. Wchnschr.* 19: 6, 1906.
2. Harabath, R.: *Gynäk. Rundschau.* 7: 705, 1913.
3. Falta, W.: *The Ductless Glandular Diseases*, Philadelphia, 1916, P. Blakiston's Son and Co., p. 378.
4. Danforth, C. H.: *Arch. Dermat. & Syph.* 3: 309, 1925.
5. Slocum, C. E.: *M. Rec.* 10: 470, 1875.
6. Hegar, A.: *Beitr. z. Geburtsh. u. Gynäk.* 4: 21, 1901.
7. Hertzfel, L.: *Wien. klin. Wchnschr.* 19: 180, 1906.
8. Jellinghaus, C. F.: *Bull. New York Lying-in Hosp.* 5: 212, 1908.
9. MacCarthy, L.: *Diseases of the Hair*, St. Louis, 1940, The C. V. Mosby Co., p. 217.
10. Ochs: *Arch. Dermat. & Syph.* 19: 693, 1929.
11. Becket, P. E.: *Arch. Dermat. & Syph.* 4: 660, 1921.
12. Trotter, M.: *Surg., Gynec. & Obst.* 60: 1092, 1935.
13. Halban, J. L.: *Wien. klin. Wchnschr.* 20: 1389, 1907.
14. Dawson, H. L.: *Am. J. Anat.* 53: 89, 1933.
15. Kirk, A. D.: Personal communication.

HYSTEROSALPINGOGRAPHY AS A DIAGNOSTIC AID IN CERTAIN TYPES OF RUPTURED UTERI

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RUPTURE of the uterus was first described by Guillemeau and since his time, numerous accounts of this serious obstetric accident have been recorded. There is no way of accurately ascertaining the number of cases of ruptured uteri or its incidence. Unquestionably, many deaths from ruptured uteri have gone unrecognized and the cause of death has been incorrectly given as "childbirth," postpartum hemorrhage, etc.

There is no great difficulty in recognizing the classical picture of ruptured uterus in pregnancy. There is usually a history of a uterine scar or intrauterine manipulation (version), sudden severe tearing pain, marked shock and prostration. In these cases the blood bank, plasma, and surgery can quickly answer the need for life-saving action. However, not all cases of uterine rupture present this picture, for the symptoms may be quite mild. These "quiet" cases can be a real diagnostic problem. This is a report of such a case, in which the use of hysterosalpingography aided greatly in the diagnosis. We feel that this diagnostic aid is a fairly safe procedure to use in such cases, and the information obtained quite valuable. For this reason, we are reporting the following case.

Case Report

This was the patient's second pregnancy. Her first pregnancy five years previously had been complicated at term by a prolapsed cord. A classical cesarean section was done, and a live baby obtained. Her post-operative course was quite stormy, peritonitis developed and only after several transfusions and a prolonged period of hospitalization did she survive.

The prenatal course of her second pregnancy was uncomplicated until the beginning of the ninth month. At this time, she began to have a moderately severe backache and was advised to go to the hospital. She arrived there about four hours later, and just before admission, the pain disappeared. At that time, her blood pressure, pulse and respirations were all within normal limits and her general physical condition excellent. That evening she stated that she no longer felt the baby move, and no fetal heart was audible. Stilbestrol was given by mouth to sensitize the uterus with the expectation that labor would start spontaneously at any time, and the dead fetus be expelled. A flat plate taken on the fourth day showed overlapping of the fetal skull bones. As labor had not started by this time, it was decided to do a sterile vaginal examination. Little had been ascertained by rectal or abdominal examination because of obesity.

The vaginal examination revealed a mass which was thought to be the uterus, separate from the pregnancy. There was some tenderness in the left lower quadrant. At this time the possibility of the fetus being outside the uterus was first thought of, but we hesitated to do a laparotomy until we could be sure the pregnancy was extrauterine and that we were not doing a cesarean section for a dead baby.



Fig. 1.—Two and one-half cubic centimeters lipiodol. Uterine cavity well outlined.



Fig. 2.—Five cubic centimeters lipiodol. Dye beginning to pass out tear in left side of uterus.

BILATERAL, MULTILOCLAR, PSEUDOMUCINOUS CYSTS OF OVARIES NECESSITATING CESAREAN SECTION

A. HERBERT KANTER, M.D., COLUMBUS, OHIO

MRS. L. B., aged 26, a white woman, called at my office on March 8, 1944, complaining of severe pain throughout the entire abdomen and back, and extending down both thighs, but more marked in the right and left iliac regions.

The patient had a great deal of difficulty in sitting down and also had difficulty in breathing.

A hypodermic of morphine sulfate had to be administered to relieve pain.

The first symptom occurred October 5, 1943, which was severe abdominal pain. The patient was ordered to the hospital by her physician, who felt that she was about six months pregnant, judging by the size of the abdomen, and that she was going into premature labor. She was symptomatically treated.

She told her physician that it was impossible that she should be six months pregnant, due to the fact that she had last menstruated August 10, 1943.

After six days' hospitalization, she was again seized with severe abdominal pain and vaginal bleeding. She called another physician, who sent her into the hospital. Because of the size of the abdomen, which had the appearance of an eight months' pregnancy, an attempt was made to induce labor, but when the above symptoms stopped, she was sent home.

The patient began menstruating at the age of nine. Periods were at regular intervals of 28 days, lasting 4 days. The amount of flow was moderate. She last menstruated on August 10, 1943.

The patient was married at the age of 17, and has been married eight years. She is a para iv. At the age of 19, she had her first child; at the age of 21, a second; and at the age of 23, her third. They were all spontaneous deliveries.

My examination revealed a well-developed and fairly well-nourished individual; six feet three inches in height, weighing 141 pounds, with fair skin and light hair.

The physical examination was entirely negative, except that I found the uterus extending up to the ensiform cartilage.

The individual had a marked fullness and protrusion of both the right and left lower abdominal regions. The right side was more marked and protruded considerably. It formed a round mass about the size of a child's head. The masses in these regions seemed fixed, but the uterus was freely movable from below.

The chest was normal throughout, the breasts were well developed, and rather soft. The heart and lungs were negative. The blood pressure was 126/75.

The abdomen was rather long, and the pelvis wide and broad. The skin of the abdomen was very tense and glistening, due to the excessive stretching. There was marked bulging and fullness in the right and left pelvis, caused by bilateral masses which were freely movable.

No fetal heart was heard. The fetus was not palpable below the umbilicus but was palpable above. There was an area of dullness on percussion in the lower two-thirds of the abdomen. The rectal examination revealed nothing. On vaginal examination, the perineum was slightly relaxed and a small cystocele was present. The cervix was long and of firm consistency. There was no ballottement, as the masses on both the right and the left side seemed to be crowding the uterus and pushing it posteriorly and upward.

The urine was negative. Blood coagulation time: 3 minutes. Erythrocytes: 5,800,300. Leucocytes: 8,200. Large lymphocytes: 58 per cent. Large mononuclears: 2 per cent. Polynuclear: 2 per cent. Neutrophils: 40 per cent. Eosinophiles: 2 per cent. Wassermann and Kahn tests were negative. X-ray, taken of both abdomen and pelvis, revealed a fairly large child, vertex presentation. The pelvis was normal and ample.

The termination of the patient's pregnancy was calculated as between May 15 and 20, 1944. But on May 5, due to increased pain and enlargement of the abdomen, I sent the patient to the hospital where she was prepared for operation. A spinal anesthetic was administered. Following this, the patient was given $\frac{1}{320}$ grain of ergotrate, intramuscularly. A midline incision was made above the umbilicus and extending down to the symphysis. The abdomen was opened in the usual manner.

Through a longitudinal incision into the uterus, which was slightly contracted, a podalic extraction was performed. The child, a male, weighed 9 pounds, 7 ounces. Another $\frac{1}{320}$ grain of ergotrate was injected into the uterus, and the placenta removed manually. The uterus was closed in the normal manner.

Examination of the right pelvis disclosed a large cystic ovary on a twisted pedicle. The blood vessels were much enlarged and marked varicosities present. Both ovarian cyst and tube were removed.

The left side also revealed a large ovarian cyst, which was removed.

The pathologic findings were the following: The left tube was somewhat stretched over a cystic ovary and measured 12 cm. in length by 6 mm. in diameter. It was smooth, straight, somewhat congested, and apparently patent. The ovary measured 15 by 13 by 9 centimeters. The external surface was smooth and round, slightly injected, and slightly hyperemic. On section, the ovary was found to be cystic and to consist of two cavities, each filled with thick pseudomucinous material, and one containing flakes of blood pigment. The inner surfaces of the thin walls were smooth. The right tube was stretched over an ovarian cyst and measured 12 cm. by 5 millimeters. It was similar in appearance to the one first described. The ovary measured 22 by 15 by 5 centimeters. The external surface was irregular, and presented injected vessels. On section, this ovary likewise was found to be cystic and to contain three cavities, each filled with clear, pseudomucinous material. The inner surfaces were smooth and the walls were thin.

Microscopic.—Sections from each ovary presented cysts lined with a single layer of tall columnar, mucous-secreting epithelial cells. The cyst wall was composed of collagenous connective tissue stroma and

some ovarian stroma. There was no evidence of anaplasia, invasion or malignancy. Sections of tubes showed them to be somewhat compressed, with empty lumina. The plicae were slightly edematous, and showed slight lymphocytic infiltration.

This patient had never complained of any pain or noticed any enlargement, and the pregnancy seemed to have stimulated the growth of these ovarian cysts. No doubt, had the rate of growth been more rapid, the pregnancy would have been terminated much earlier.

Had she been permitted to deliver by the vaginal route, it is very evident that there would have been a rupture of either of the ovarian cysts, causing internal hemorrhage due to the increased size of the blood vessels and resulting in the death of the patient.

The mother and child had an uneventful recovery, and left the hospital on the tenth day.

558 EAST LIVINGSTONE AVENUE

X-RAY STUDIES IN HYSTEROSALPINGOGRAPHY, USING A NEW CANNULA

A. P. HUDGINS, M.D., CHARLESTON, W. VA.

THE use of a new cannula, devised by the writer, for hysterosalpingography, requires slightly different x-ray interpretation when the films are read.

This new, indwelling, self-retained, valve cannula can be inserted in the physician's office, the opaque medium injected and the patient allowed to walk to the x-ray room for the film. She then returns for the removal of the cannula and the procedure is complete.

The Colvin, screw-type cannula has been modified by the author by inserting a valve device, and by making the handle detachable. The valve maintains intrauterine pressure and the removable handle makes the examination an ambulatory office procedure. (Fig. 1.) The opaque medium is injected with a regular Luer-type syringe; the tip fitting into the large end of the cannula after removal of the handle.

The use of this cannula has been found to simplify the procedure of hysterosalpingography and it is hoped that wider use will be made of this more complete and detailed method in sterility investigation.

Technique of Insertion of the Cannula

There are a few modifications of the routine procedure which may be helpful to note. The patient is put in the usual stirrup position; a bivalve speculum inserted and sterile preparation of the vagina and cervix is carried out. The cervix is then sounded with a regular number 13, curved cervical dilator. The special indwelling, retained cannula-with-valve is then inserted by clockwise rotation. When it has been inserted as far as possible, so that it becomes firmly fixed in the cervix, the handle is removed and about 6 c.c. of the warmed opaque medium* is injected. The syringe is detached and the cannula is given one more turn to make sure that it is securely held within the cervix. The vagina should be sponged out to remove any of the opaque medium which may have leaked out into the vagina and which may cause confusing shadows. A regular tampon, with string attached, is left in the vaginal vault to absorb any remaining opaque medium. Instructions are given that this tampon is to be removed before the flat plate is taken. The patient is then instructed to be up and about, and a note is written that the plate is not to be taken for at least 30 minutes after injection has been completed. The purpose of this interval is, of course, to allow the medium to be worked out into the tubes by the muscular contractions of the uterus. If enough time elapses, only one plate will be necessary, thus obviating the necessity of the additional time-consuming procedure of the two-hour and the 24-hour plates.

During the early part of the work, the writer advised the use of the vibrator, applied to the abdomen, to make sure that the medium was ex-

*Iodochloral (Searle) employed.

pelled and forced out of the tubes, unless obstruction was present. The use of this vibrator, however, has been found to be rarely necessary. The 30-minute time interval, allowing the patient to be up and about, usually accomplishes the same result.

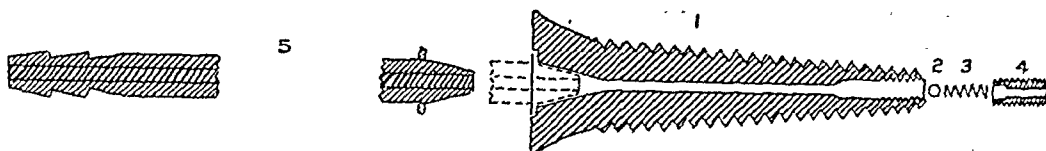


Fig. 1.—Improved cervical cannula. 1. Cannula. 2. Ball valve. 3. Valve spring. 4. Valve plug. 5. Stem.

Interpretation of Plates

With this method, using the new cannula, one plate is usually all that is required in the investigation for tubular patency. With the old method, when the picture was taken within a few minutes following the injection of the medium into the uterus (and with the patient still in the recumbent position), the uterus and a complete outline of the tubes—with, perhaps, drops free in the peritoneal cavity—were usually clearly seen. Using the new cannula, however, if the tubes are still filled well after the above-mentioned time interval, it has generally proved to be an indication that there is some obstruction. (Figs. 2 and 3.) It has been found that the unobstructed, freely movable tube does not retain the fluid for 30 minutes when the patient is up and about. (Case 1, Fig. 2.)

Gravity, the uterine and tubular contractions, and intra-abdominal pressure are all factors concerned with expelling the medium from the tubes.

A small opening would, naturally, allow a proportionate amount of the material to escape. The interpretation of the single plate, then, is more or less a combination between the first and the second plates (immediate and 24-hour plates) when using the old method. The opaque medium should be chiefly in the uterus and in the peritoneal cavity if the interpretation is to be made of completely unobstructed tubes. There may be a film-like outline, but not a full-size tube structure.

Therapy

As can be readily seen, this cannula may be retained over a period of time: not only the 30 minutes required for the x-ray procedure, but for 12 to 24 hours, or more, thus stimulating gentle, rhythmic muscular contractions of the uterus in an effort to open up an obstruction of the tubes. In this way, the special cannula can be used not only for diagnostic purposes, but also as an improved method in the effort to open obstructed tubes.

This procedure, utilizing the gentle, continuous, rhythmic, muscular contractions of the uterus over a period of time, has proved to be much more satisfactory than the old method by which pressure was increased suddenly—accompanied by pain, muscular contraction, spasm—and consequent resistance on the part of the patient. The first spasm, or muscular contraction, which comes with the initial discomfort of the injection, gradually subsides and the continued gentle (but forceful) uterine pressure appears to accomplish (over a period of time, after relaxation,



Fig. 2.—Case 1. Cannula retained, with valve. After 30 minutes, vibrator not used. Uterus outlined. No medium in tubes but free complete spill, showing tubal patency, no pathology.



Fig. 3.—Case 2. After two hours, showing medium outlining uterus, small amount at ends of tubes, free in peritoneal cavity. Tubes found closed in several previous hysterosalpingograms.

and after the initial "cramps" have subsided) what is not accomplished by short periods of more artificial, jerky, sudden injection pressure.

If necessary, the patient may be sedated in order that the initial discomfort may be less. This will insure better cooperation if several injections should prove necessary, since the patient will agree more readily to repeated injections if the pain can be reduced. (Case 2, Fig. 3.)

It is thought by some clinicians that injection of the tubes offers a better hope of correcting obstruction than can be offered by surgical means (that is, by laparotomy and salpingotomy). A case, illustrating the use of this instrument for the purpose of opening the tubes, is shown. (Fig. 3.) This is a case which, on repeated occasions, had been found (by salpingography) to have an obstruction of the uterine end of the tubes. This is, of course, the type of obstruction in which surgery offers little hope. The type of tube obstruction which offers the greatest hope of correction surgically, is the obstruction which occurs at the distal end of the tube, thus permitting the removal of a portion of the tube and cuffing back the end of the tube with the hope of preventing a recurrence of the clubbing and its consequent obstruction. The case shown, after having failed to open when the old method was used, responded to therapy with the new cannula.

This instrument has been used in over 60 hysterosalpingographic studies, over a period of more than one year. The method has been found to be simpler and much more satisfactory than the one formerly employed.

One tuboovarian abscess resulted from the injection. This was, apparently, a poorly chosen case in which there flared up an unrecognized adnexal disease that had not adequately subsided. In this case, it is believed that any method of injection would have caused the same result. The modified technique was, therefore, not considered to be a factor.

Conclusions

When employing the new technique (using new, self-retained, indwelling cannula-with-valve) for hysterosalpingography, the following points should be noted:

1. Simplification of technique.
2. One-plate method (instead of the two-or-more plates, 24-hour method).
3. Examination completed within one hour instead of 24 hours.
4. Less pain and trauma for patient.
5. Less expensive for patient.
6. More quickly and satisfactorily accomplished by physician.
7. Functional obstructions of Fallopian tubes (spasms, mucous plugs) fewer and more easily overcome because of more effective therapeutic action.
8. Films are clearer: fewer instrument shadows, thus more satisfactory interpretation.
9. Early medium spill, with instrument in place, gives better orientation.

10. An effective, satisfactory 30- to 60-minute plate makes available the lighter, more easily absorbable opaque medium base (peanut oil base).
11. Therapy: To open obstructed tubes.
 - A. More effective (because of prolonged, sustained, gentle, rhythmic pressure can be retained for 24 hours).
 - B. More easily accomplished.
 - C. More adaptable to repeated treatments (sedation may be used).
 - D. Less painful.
 - E. Uterine-tubular pressure found more effective than surgery (laparotomy, salpingotomy).
12. Film interpretation.
 - A. One plate is usually adequate.
 - B. Completely patent, freely movable tubes rarely shown fully outlined after 30-minute interval.

I wish to thank Dr. E. W. Squire, Charleston, W. Va., for his helpful suggestions and advice.

References

- Brunkow, B. H.: Uterography: An Aid in Diagnosis of Gynecologic Pelvic Disorders, *Am. J. Surg.* 61: 394-399, Sept., 1943.
- Colvin, Emmett: *AM. J. OBST. & GYNEC.* 37: 168-169, 1939.
- Fist, Harry S.: Tubal Insufflation Method, *Am. J. Surg.* 69: 143-144, 1943.
- Goldberger, M. A.: The Clinical Evaluation of Hysterography: *J. Mt. Sinai Hosp.* 10: 241-249, 1943.
- Green, V. B.: Lessons and Virtues of Salpingography, *J. Obst. & Gynaec. Brit. Emp.* 50: 23-26, 1943.
- Kolbow, H.: Uterus and Vagina in Lateral Roentgenogram, *Zentralbl. f. Gynäk.* 65: 748, 1941. *Abstr. AM. J. OBST. & GYNEC.* 46: 472, 1943.
- Leinzinger, E.: *Röntgenpraxis* 12: 389-392, 1940.
- Leinzinger, E.: *München. med. Wchnschr.* 87: 1023-1026, 1940.
- Leon, Charles T.: Dermoid Cysts of the Ovary; Roentgen Diagnosis in Pregnant and Nonpregnant Women, *Arch. Clin. obst. y ginec. "Eliseo Cantón"* 2: 93-118, 1943.
- Leventhal, Michael L., and Solomon, Ernest M.: *AM. J. OBST. & GYNEC.* 41: 628-640, 1940.
- Millen, Robert S., and Jones, Elwood: *AM. J. OBST. & GYNEC.* 41: 340, 1941.
- Mocquot, Palmer R., and Pulsford J.: *Rev. franç. de gynéc. et d'obst.* 36: 1-9, 1941.
- Robberson, J. H.: Fallopian Tube Visualization, *Texas State J. Med.* 39: 340, 1943.
- Rosado, J., and Normoraes, A.: Hysterosalpingography in the Diagnosis of Ectopic Pregnancy, *Obst. y ginec. latino-am.* 1: 19-30, 1943.
- Rubin, I. C., and Morse, Arthur H.: *Am. J. Roentgenol.* 41: 527-536, 1939.
- Rubin, I. C.: Clinical Differential Demonstration of Uterine and Tubal Contractions by Kymographié Uterotubal Insufflation, *AM. J. OBST. & GYNEC.* 45: 419-431, 1943.
- Schneider, Paul: The Problem of the "Tubal Sphincter" and of the Intramural Portion of the Fallopian Tube, *Am. J. Roentgenol.* 48: 527-542, 1942.
- Stein, Irving F.: X-ray Diagnosis in Gynecology, *S. Clin. North America* 23: 165-180, 1943.

A NEW SELF-RETAINING VAGINAL RETRACTOR*

For Postpartum Cervical Inspection and Repair

EUGEN GUTTMANN, M.D., LOS ANGELES, CALIF.

(From the Obstetrical Department of the Cedars of Lebanon Hospital)

POSTPARTUM cervical inspection and repair are difficult unless the cervix can be well visualized. There has been great need for a cervical speculum which provides good exposure of the cervix and retains itself in the vagina so that it cannot be displaced by such movements as vomiting, or by manipulations such as traction on the cervix. Such an instrument should be simple in construction and easy to control.

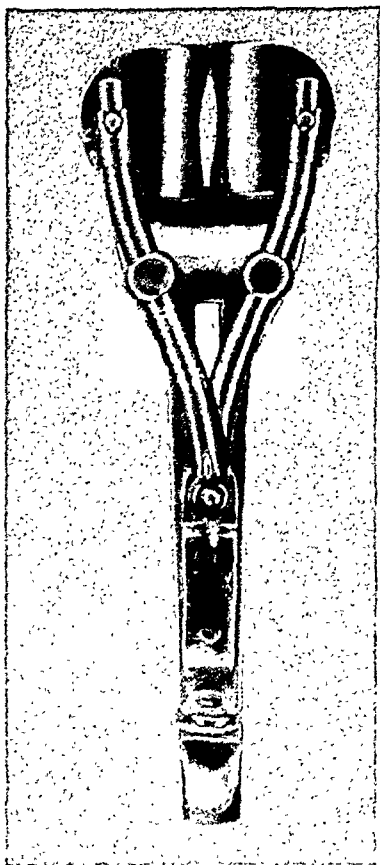


Fig. 1.—Retractor closed.

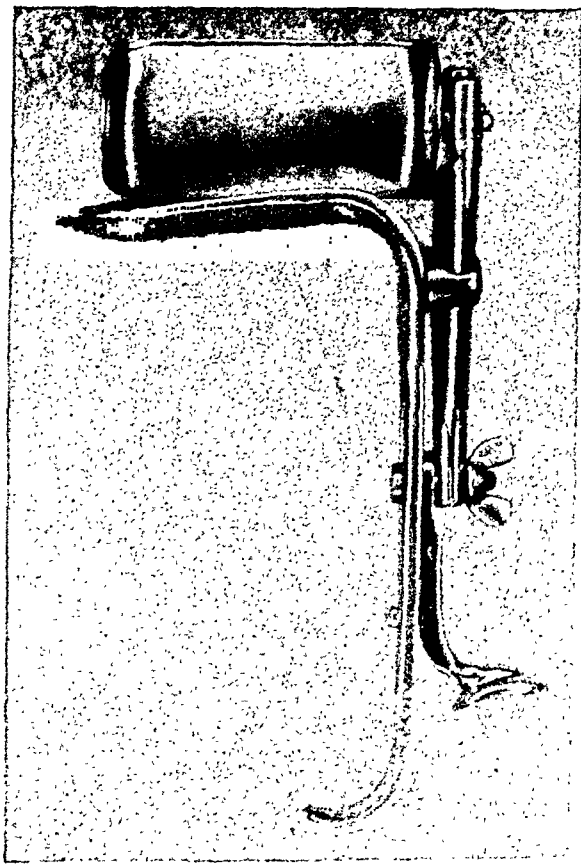


Fig. 2.—Retractor closed, seen from side.

During the past two years, the retractor here described has been used satisfactorily at the Cedars of Lebanon Hospital by approximately 20 obstetricians, on several hundred cases. It provides adequate visualization of the cervix and retention of the retractor without injuring the tissues. It may be opened to any desired width and retains itself securely.

*The new retractor is manufactured by Woods Professional Supplies, manufacturers of surgical instruments, 8442 Otis Street, South Gate, Calif.

The retractor consists (Figs. 1-3) of a relatively broad base-plate on which are arranged two broad rotatable side-blades. The side-blades are mounted on two rods, by means of which they can be pushed upward and outward, gently unfolding the vaginal walls and adapting themselves to the individual shape and direction of the pubic bones of this patient. The greatest possible width can thus be reached in each individual case regardless of whether the pubic arch be wide or narrow.

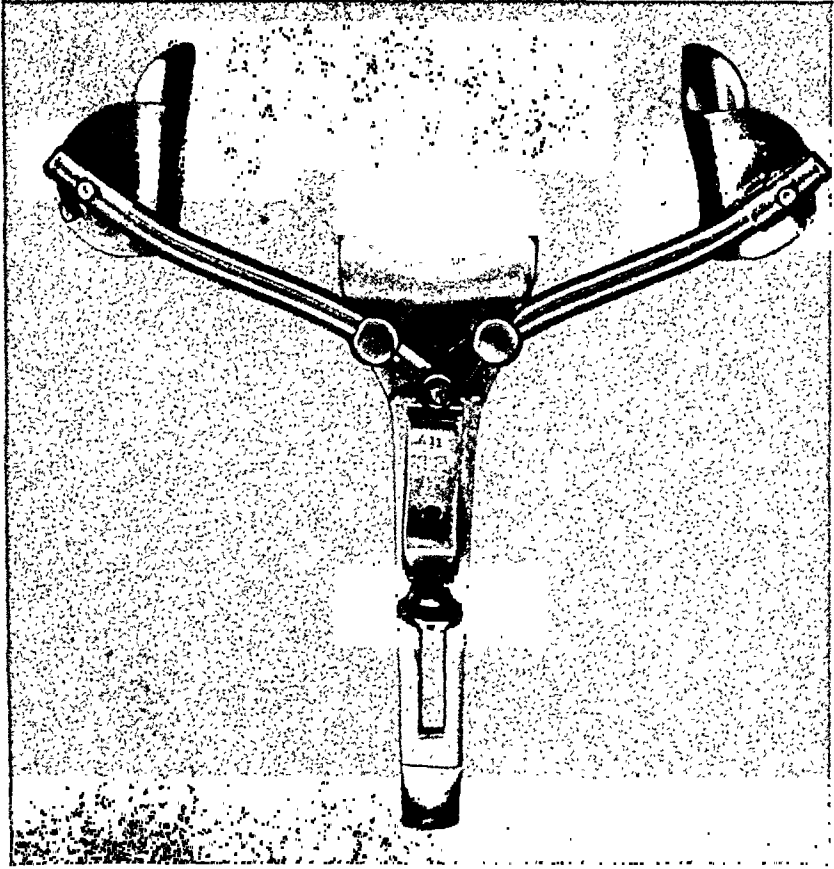


Fig. 3.—Retractor opened. Pressure of the thumb on the movable slide opens the retractor to the desired width. Tightening of the thumb-screw fixes the retractor in position.

The three-way movement of the blades provides an equal and symmetrical opening whereby the side-blades are brought in approximation with the pubic bones without exerting any pressure thereon. The side-blades are provided at their ends with hooks broad enough to anchor them firmly behind the pubic bones. The side-blades and base-plate open synchronously so that the retractor opens and retains itself at one movement. It needs no interchangeable side-blades of different length as it does not depend on the individual length of the vagina. Instead of attempting to hold itself by pressure against the soft mobile vaginal walls, it is held firmly behind the pubic bones.

This new obstetric self-retaining vaginal retractor should be especially helpful to obstetricians since the scarcity of interns and nurses makes operating without assistants the rule instead of the exception.

PLACENTA DELIVERED FIVE HOURS BEFORE BIRTH OF THE FETUS

RICHARD TORPIN, M.D., AUGUSTA, GA.

(From the University Hospital)

FOR a proper understanding of prolapse of the placenta (i.e., its delivery prior to the birth of the fetus), one should study the classic papers by J. Y. Simpson, Rucker, Bureczak, and Kobak and others, who have made more or less comprehensive analyses of the subject, besides reporting cases. J. Y. Simpson experimented with the idea of reducing maternal mortality in placenta previa centralis by manually removing the placenta in these cases before the delivery of the fetus.

Incidence of spontaneous prolapse of the placenta is extremely rare. In 8,000 supervised deliveries it has occurred only this once, and in 20,000 others delivered in this University Hospital over the past twenty-five years, my associates remember only one or two cases. Rare as it is, a well-trained obstetrician should have it in mind, and if it occurs when he is prepared for delivery, he may rapidly complete the second stage of labor with successful outcome for the fetus, as reported in two cases by Kobak and his associates.

In case the fetus is not viable or is dead, the treatment should be conservative for the sake of the mother unless there is maternal hemorrhage which probably is controllable by the onset of intensified labor contractions which force the presenting part into the cervical canal. A tight abdominal binder is of value also.

Other than in placenta previa centralis the most likely time for prolapse to occur is in the case of twins after the delivery of the first infant and before the birth of the second twin. In these cases manual delivery of the second twin by deep episiotomy and Kristellar expression or forceps, if presentation is cephalic, or by extraction if breech, or version and extraction if transverse, are the procedures of choice.

In all cases where a live infant is born, it may be in a state of partial to complete anoxia, and it is well to have at hand for immediate use an intratracheal catheter and an insufflator with a pressure control of 20 cm. of water (14 Hg.). If the fetus is markedly premature or already dead, and presents by head or breech, and there is slight vaginal hemorrhage, management by spontaneous delivery is safest for the mother from a standpoint of danger of infection and injury to the cervix. During the interval between delivery of the placenta and delivery of the fetus, the attendant should constantly observe the amount of vaginal hemorrhage and the progress of the presenting part which, when deeply engaged, successfully prevents further hemorrhage. In all cases, lost blood should be replaced immediately by transfusions.

Case Report

M. L. D., Negro female, aged 26, weight 125 pounds, height 5 feet, 4 inches, small stature, had her last menstrual period February 2, 1944, and had felt life in June. On August 19, she began to bleed vaginally, more so at night than in the daytime and continued this to

August 25, when, at 3:00 P.M., she began to have uterine contractions and labor pains, which proceeded as in labor to 10:28 P.M., when she expelled the placenta without the membranes. The fetus remained in the uterus which contracted firmly around it.

Her blood pressure then was low, 60/40, due no doubt, to protracted blood loss, although there was only moderate hemorrhage at the time of delivery of the placenta or thereafter. She had entered the hospital with marked anemia, R.B.C. 2,670,000 and 8 Gm. hemoglobin, per 100 c.c., but because of her proving to be Rh negative, she had not received any blood transfusions.

However, because of her surgical shock condition following delivery of the placenta, she was given 1 pint of matched blood. Besides this, the treatment consisted of a tight abdominal binder and constant administration of oxygen by nasal tube. Approximately five hours later, at 3:10 A.M., August 26, she expelled the six months' stillborn female fetus which weighed 2 pounds, 2 ounces (963 Gm.), and was covered by the amnion. The fetus was not malformed, nor erythroblastotic. The placenta was circumvallate in process of formation. It measured 10 by 16 cm., and weighed 215 grams. The cord, 40 cm. long, was attached to the placenta eccentrically. The placenta had no gross appearance of erythroblastosis; it had one edge slightly darker in color on the fetal surface. There were no gross areas of infarction. The placenta probably was low lying, or even may have covered the internal os as in central placenta previa.

Lateral x-ray on August 23, revealed a six months' fetus in transverse presentation rather high in the uterus, with thin uterine wall shadow front, back and over the apex. From these facts, one can conclude that the placenta was entirely below the fetus at the time of making the x-ray film, two days before the onset of labor. She recovered without complications.

References

1. Simpson, J. Y.: *Month. J. M. Sc.* 158: 169, 1845.
2. Simpson, J. Y.: *Selected Obstetrical and Gynecological Works*: Edited by Dr. J. Watt Black, J. Appleton and Co., New York, 1871.
3. Rucker, M. P.: *AM. J. OBST. & GYNEC.* 11: 189, 1926.
4. Burzeak, H.: *Zentralbl. f. Gynäk.* 58: 1829, 1932.
5. Kobak, Alfred J., et al.: *AM. J. OBST. & GYNEC.* 42: 330, 1942.

FETUS ADIPOCERE MONSTER

JOHN JOSEPH GILL, M.D., CHICAGO, ILL.

(From the Illinois Central Hospital)

ADIPOCERE is designated as a peculiar waxy substance formed during the decomposition of animal bodies, seen especially in human bodies buried in moist places. It consists principally of fatty acids and their salts called "grave-wax."

Mrs. F., aged 35 years, weighed 270 pounds. Her weight was 136 pounds ten years ago. Her menstrual periods began at the age of thirteen and were regular thirty-day type, lasting two days except during her pregnancies.

She has delivered four normal living children, each weighing eight to ten pounds at birth; the youngest is ten, the eldest sixteen years old; one spontaneous five-month abortion resulted from a fall four years ago.

Her last menstrual period occurred May 13, 1941, and considering herself in the menopause state, she did not consult her physician until the latter part of November.



Fig. 1.—Anterior view of fetus adipocere monster.

Dr. E. A. Wuesterman, without examining the patient, referred her to me for a diagnosis and treatment. I first saw her on December 15, 1941. Her ponderous abdomen, distended in every direction, was too firm to outline any contents within its boundary; vaginal examination gave only evidence of a thick, soft cervix. Three x-ray plates were taken before a faint shadow of an apparently abnormally developed, large fetus could be outlined.

The patient had not felt life at any time during this pregnancy, no fetal heart tones or movements could be elicited at this time. I decided for the present to keep her under observation and to await results.

On December 23, she developed painful contractions and entered the Illinois Central Hospital at 10:25 P.M. During her obstetric preparation

at 2:30 A.M., the membranes spontaneously ruptured and literally flooded the room, after which some hard, immobile, immovable, fetal body could be outlined within the uterus. The cervix was dilated to 3 cm. and the pains ceased. Quinine and castor oil did not assist labor.

After forty-eight hours from the beginning of labor pains, she developed a temperature of 102° F., blood pressure 90/60, red count was 3,610,000 and whites, 8,500.

December 26, after consultation with Drs. Charles M. Laury and Wm. T. Carlisle, a cesarean section was agreed upon and the following condition was found to exist: a mottled brown, statue-like figure of firm, almost brittle texture was adherent to the endometrium, which required blunt dissection to separate.



Fig. 2.—X-ray of fetus adipocere monster.

Upon attempting to remove the fetus, a hand snapped off at the wrist and likewise the right leg at the knee; there was no bleeding from these broken surfaces.

The female monster, resembling a wax doll, weighed eight pounds, measured 36 cm. from crown to rump, both feet and hands were clubbed, the cranium contained fluid and very little brain substance. The large placenta weighed one and three-quarters pounds.

The uterus with one tube and ovary was removed, followed by a stormy, septic fever for three weeks. The patient was discharged from the hospital on February 1, 1942, forty-two days after admission. She has remained in excellent condition at her last report of August, 1944.

The references consulted, mostly medicolegal and few in number, do not include any instances of fetal adipocere developing in utero.

Department of Reviews and Abstracts

Selected Abstracts

Labor, Physiology, Management, Complications

Radcliffe, Walter: *The Blood Pressure in Labor*, Brit. M. J. 4340: 354, 1944.

The author is of the opinion that since barbiturates produce a hypotension, they should be used only in the early stages of labor, and they are best avoided within a short time preceding delivery. Hypotension during the third stage of labor is to be regarded as a danger sign, and the blood pressure should be restored before anything else is done. It is strongly urged that the sphygmomanometer be an important adjunct in the care of a woman during labor.

WILLIAM BERMAN.

Norton, W. A.: *Inversion of the Uterus*, Am. J. Surg. 63: 408, 1944.

After pointing out the rarity of inversion of the uterus, the author describes 2 cases. The first was seen some hours after its occurrence during delivery, attempts at reduction were unsuccessful, and the patient expired. In the second case, the inversion had also occurred during delivery, but was present for 6 months before admission to the hospital. The patient was markedly anemic and after repeated transfusion and other supportive measures had been utilized, a vaginal hysterectomy as the operation of choice was decided upon. In order to reduce hemorrhage to a minimum, the author used a tonsil snare over the wire of which a small rubber boot had been fashioned to grasp the inverted fundus almost to the level of the constricted cervix. When the rubber-protected snare was tightened, it acted both as a tourniquet and a tenaculum allowing the inverted fundus to be pulled well down so that it could be quickly removed with the electric cautery. The stump was sutured and pushed through the constricted cervix. The patient's convalescence was uneventful. The author recommends the use of the tonsil snare as described in similar cases.

FRANK SPIELMAN.

Welton, T. S., and Ellingson, O.: *Pregnancy and Delivery With an Intrauterine Pessary in the Cervix*, Am. J. Surg. 54: 484, 1941.

A case is reported of spontaneous delivery of a 2-pound, 6-ounce baby in a 37-year-old white gravida 8, who had worn a stem pessary continuously for 6 months prior to her pregnancy. Her membranes ruptured spontaneously 2 months before term, and at the time of admission, a moderate intrauterine infection was noted. The fetus was delivered easily and the stem pessary was found embedded in its scalp. It was removed without difficulty leaving a noticeable but transient impression of the appliance. Both mother and infant survived.

FRANK SPIELMAN.

Robertson, H. E., and Dochat, George R.: **Pregnancy and Gallstones**, Internat. Abst. Surg. 78: 193, 1944.

An extensive and complete historical review of the correlation between gallstones and pregnancy is herein presented. The commonly accepted statement that 90 per cent of women who have gallstones have borne children is traced to Naunyn's pupil, Heinrich Schroeder. The authors point out that these original figures are open to serious question because of an insufficient number of cases and are not suitable to the statistical conclusions derived from them.

It is further pointed out that to establish the predisposing effect of pregnancy on the production of cholelithiasis, it must be demonstrated that the percentage of gallstones in women with children is appreciably greater than the percentage of women who bear children in the population at large. When the figures of the present authors and their predecessors are analyzed on this basis, it is found that 79.25 per cent of all women have borne children. This figure corresponds very closely with the number of women with gallstones who have borne children. Therefore, while the percentage of women with cholelithiasis is 2 to 3 times that of men, there is no statistical evidence whatsoever that the phenomenon is related to childbearing.

L. M. HELLMAN.

Newborn

Bulfamonte, J. C.: **Large Ovarian Cyst in Newborn Child**, Am. J. Surg. 55: 175, 1942.

This is a case report of a large ovarian cyst in a newborn infant recognized at birth, and soon after delineated by x-ray. Laparotomy was performed at the age of 5 weeks, and a neoplasm filling the entire abdomen and requiring aspiration was found. It arose on a long pedicle from the left ovary and was easily removed. A smaller cyst "about the size of an orange seed" was also removed from the right ovary. The pathologic report was cystadenoma.

FRANK SPIELMAN.

Bakwin, Harry, and Patrick, Thomas W., Jr.: **The Weight of Negro Infants**, J. Pediat. 24: 405, 1944.

The authors report a study of 114 Negro infants, making 679 observations from early life. On standard diets, these infants showed no significant difference in weight gain than white children during the first year of life, and that given proper medical supervision, Negro infants from moderate income families grow as well as white infants.

JAMES P. MARR.

Hardwicke, Sarah Hooker: **Studies on the Minimal Effective Dose of a Water-Soluble Vitamin K Substitute in the Prevention of Hypoprothrombinemia in the Newborn Infant**, J. Pediat. 24: 259, 1944.

A total of 87 breast-fed newborn babies were studied in an attempt to establish an approximate minimal effective daily dose of synkayvite (tetra sodium 2-methyl-1,4-naphthohydro-quinone diphosphoric acid ester).

They were divided into six groups, of which infants in five received doses of 0.5, 0.05, 0.005, 0.0005, 0.00005 mg. of the test substance daily, and infants in one of which served as controls. The substance was given orally.

The minimal dose of 0.0005 mg. given daily would probably prevent the development of hemorrhagic disease, except in a few cases. Approximately 1.25 mg. of the

test substance is apparently effective in lowering an excessively high prothrombin time to a normal range, i.e., 20 to 75 seconds; the danger zone lay between 70 and 100 seconds.

The administration of secenal, nembutal, and sodium amytal to mothers of the babies studied in this series had no demonstrable effect in prolonging the prothrombin time of the babies. Of interest was the baby born from a mother with a placenta previa, and an estimated hemorrhage of 500 c.c. of blood. This prothrombin time was 135 seconds. Mineral oil administered orally has been shown to lower the blood prothrombin of experimental animals.

JAMES P. MARR.

Potter, Edith L.: A Double Ova Pregnancy in Which the Rh Positive Twin Developed Erythroblastosis, J. Pediat. 24: 449, 1944.

An interesting case is reported of twins, one of whom died of erythroblastosis while the other remained normal. The affected twin and the father were Rh positive, the normal twin and the mother were Rh negative.

It is contended that the father was heterozygous for the Rh factor and that two ova were fertilized, one by a sperm carrying Rh-positive gene and the other a sperm carrying an Rh-negative gene. The Rh-negative mother had been sensitized to the Rh factor either in the previous pregnancy, when an Rh-positive fetus had been carried, or possibly during the course of this pregnancy by the Rh-positive twin.

The fetus whose cells were agglutinated developed erythroblastosis. The one whose cells were not agglutinated remained well.

JAMES P. MARR.

Pregnancy, Complications

Bottiroli, Ernesto: Diagnosis of Fetal Death by Determination of Coagulation Time of Maternal Blood, Bol. Soc. de obst. y ginec. 22: 464-470, 1943.

The author states that coagulation time of normal gestating women varies between 12 minutes, 15 seconds and 15 minutes, 18 seconds. In 32 patients carrying dead fetuses in the last trimester of pregnancy, he found that the coagulation time was about 5 minutes. In 10 women with dead fetuses in the earlier stages of pregnancy, the coagulation time was at least twice as long. But in all cases seen 12 to 21 days before expected delivery, there was a striking reduction in coagulation time (10 to 13 minutes below the normal value). Hence, in doubtful cases of fetal death, determination of coagulation time is a useful procedure. Diagnosis is definite if the time is around 5 minutes. The method can be used only in the last three months of pregnancy.

J. P. GREENHILL.

Duek, H.: Hemotherapy in Pernicious Vomiting, An. brasil. de ginec. 17: 197-203, 1944.

The author treated 100 cases of pernicious vomiting of pregnancy by means of autohemotherapy. The patients were given daily injections of 10 c.c. of blood for three successive days. Satisfactory results were observed in 94 cases. The remaining six patients were relieved by auto-urine therapy. Symptoms other than vomiting were also relieved. There were recurrences of vomiting in 10 cases. A second course of autohemotherapy was given with success. Two patients had 3 courses of treatment.

J. P. GREENHILL.

Zuckermann, C.: Uterine Myoma and Pregnancy, Rev. mex. de cir., ginec. y cáncer. 11: 307-312, 1943.

The author describes a primipara, 28, in whom pregnancy occurred despite the presence of a large myoma between the cervix and body of the uterus. A living child that weighed 3 kg. was delivered by cesarean section, since the large tumor prevented a natural delivery. Suppurative and gangrenous metritis and an intra-peritoneal abscess developed, which, with the large tumor, necessitated subtotal hysterectomy. Appendectomy also was performed, since the appendix was adherent to the uterus. The patient recovered satisfactorily. The wound was closed with drainage after extirpation of all the lesions and local application of 6 Gm. of sulfathiazole intraperitoneally.

J. P. GREENHILL.

Eckerson, E. B.: Primary Ovarian Pregnancy, Am. J. Surg. 54: 487, 1941.

In 339 cases of ectopic pregnancy seen at the St. Luke's Hospital, New York City, during the past 40 years, there was only one case of primary ovarian pregnancy, an incidence of 0.2 per cent. The case is here presented. It occurred in a 38-year-old gravida i, para 0, whose previous pregnancy terminated in miscarriage 20 years before. There was no skipped period since her last menstruation had taken place 2 weeks before the onset of symptoms. The clinical picture was that of a ruptured Graafian follicle with intra-abdominal hemorrhage. At operation, the tube was uninvolved and the ovary was the site of what appeared to be a ruptured follicle bleeding actively. A salpingo-oophorectomy was performed. Pathologically, the tube was normal, and the ovary showed the ovarian pregnancy which satisfied the requirements as postulated by Spiegelberg and by Williams and Norris. No corpus luteum was found in either ovary.

FRANK SPIELMAN.

Da Costa, L. A. Correa: Myomectomy and Pregnancy, An. brasil. de ginec. 16: 438-441, 1943.

The author reports a case of myomectomy during the fifth month of pregnancy, followed by spontaneous delivery at term. The incidence of this association is variously given as from 0.03 to 0.7 per cent, but among 1,661 maternity cases the author observed 25 of myoma, or 1.5 per cent, possibly because 58.8 per cent of the patients were colored or mulattoes.

Of the 25 cases, 13 were diagnosed only during the puerperium, 6 during labor and 6 during pregnancy. Five were operated upon: one each for hemorrhage of the pedicle, pains and coexistence of ovarian cyst, obstruction of the pelvic canal and lack of space. The patient with obstruction of the pelvic canal had a Porro operation; the other interventions were simple myomectomies during pregnancy. There was no interruption of pregnancy or any serious complication during labor or the puerperium.

The author's opinion favors the view that present obstetric resources allow an expectant attitude toward these cases. Surgical intervention is imperative when complications arise, such as necrobiosis, torsion, hemorrhage, compression, uterine incarceration, etc., or when there is lack of space as with large myomas. In these cases, the operation should always be myomectomy when possible. Hysterectomy is reserved for infected cases, those in which myomectomy is technically impossible, or in which the uterine cavity or the membranes have been accidentally opened.

J. P. GREENHILL.

Noyola, J. N.: *Clinic of the Dead Fetus*, Rev. de cir. mex. 15: 417-424, 1943.

The author classifies the causes of death into maternal (general and local) fetal and ovular; in some cases the cause remains unknown. In 20 cases collected by him, the cause was syphilis in seven, intoxication of renal origin in four, typhoid pneumonia, malaria, placenta previa, decidual endometritis and thrombosis of the vessels of the umbilical cord in one each, and unknown in three.

If the fetus is expelled during the first hours after its death, it shows no changes; if weeks or months pass before expulsion, the changes range from dissolution to mummification and maceration of varying degrees. During any of these changes, the fetus may become infected, especially by anaerobes which produce putrefaction.

The symptoms vary with the period of pregnancy during which the fetus dies. Auscultation is of great value. When the fetus putrefies, symptoms of intoxication appear in the mother, and percussion reveals tympany of the uterus due to the gases of putrefaction which usually escape through the vulva. The laboratory may be of great help in making or confirming the diagnosis. Fetal death is immediately followed by a considerable decrease in the gonadotropic hormone of the blood and urine. Roentgenography furnishes important data, especially in the last months of pregnancy (overriding of the cranial bones and exaggerated flexion of the vertebral column).

During labor, the fetus may show signs of asphyxia, such as cardiac changes, altered fetal movements and evacuation of meconium, which indicate immediate intervention.

When death of the fetus is diagnosed, treatment must be individual, although some general rules can be established on the basis of the stage of the pregnancy and the changes in the fetus. During the first three months of pregnancy, spontaneous abortion occurs in the first few days following fetal death. If the fetus is retained, spontaneous evacuation is awaited, unless the membranes are ruptured (limited waiting), or the fetus becomes putrefied (immediate evacuation; total hysterectomy if the mother shows signs of grave infection).

When it has been impossible to determine the cause of the fetal death, it is advisable to treat the case with vitamin E in sufficient and prolonged dosage. The use of oxytocics should be limited and prescribed exclusively by physicians.

J. P. GREENHILL.

Delascio, D., and Rudge, W. de Souza: *Dystrophia-Dystocia Syndrome*, An. brasil. de ginec. 16: 415-427, 1943.

The authors report two cases and stress the necessity of a wide knowledge of this pathologic obstetric picture. The term of dystrophia-dystocia syndrome was used by Greenhill in an article published in *Surgical Clinics of North America* in 1924. He called attention to the relative sterility of these patients, and stated that frequently they conceived only once and late in life. Their external aspect is heavy with short extremities and masculine and hyperpituitary characteristics. The pelvis is narrow and there is a familial history of dystocia. Their pregnancies go beyond term, frequently present early rupture of the membranes with irregular contractions, and the position of the fetus is occipitoposterior. Greenhill described seven cases and recommended the low, cervical cesarean section for these patients.

According to DeLee, the syndrome is characterized by the following manifestations: 1. Pelvis of male type or slightly justo minor, with obesity localized to the trunk and roots of the extremities and simultaneously other signs of adiposogenital dystrophy, small cervix and narrow rigid vagina. 2. Late primiparity. 3. Hypermaturity of the fetus (prolonged pregnancy). 4. Absence of engagement

of the fetal presentation when labor begins. 5. Occipitoposterior position. 6. Early or premature rupture of membranes. 7. Weak contractions with prolongation of the first stage of labor. 8. Familial dystocia. 9. Tendency to eclampsia. He points to the numerous mechanical difficulties which may arise in these cases during labor. He states that, owing to genital hypoplasia, frequent in these cases, delivery by the vaginal route is accompanied by extensive lacerations of the cervix and other soft parts and that uterine atonia often occurs. Finally, after delivery, he often felt that, if these difficulties could have been foreseen, cesarean section would have been the best course from the beginning.

It would seem that the syndrome is found once in 200 labors, or once in 80 labors of primiparas. It occurs in the various women of the same family, and the patient frequently is an only daughter. The diagnosis offers no difficulty for those who remember the typical clinical characters of the disease which have been stressed by all authors who have treated the subject. Unfortunately, the diagnosis is rarely made in daily practice, and this results in disastrous consequences for mother and fetus: for the former, lacerations, puerperal infection, psychoses, etc.; for the latter, high mortality and, in those who survive the traumatizing labor, the results of intracranial hemorrhages.

Considering the poor prognosis of vaginal delivery, the authors insist on cesarean section as the only therapeutic method.

J. P. GREENHILL.

Vaccaro, H., and Meza, A.: Hemoagglutinin Rh and Fetal Erythroblastosis, First Investigations Made in Chile, *Rev. chilena de pediat.* 10: 717-733, 1943.

The authors studied the Rh factor in 172 individuals and, after elimination of those connected with erythroblastosis, found 92.5 per cent of Rh positives and 7.5 per cent of Rh negatives. The percentages of Rh positives in the white race of the United States are 85.

The typical combination of Rh-negative mother and Rh-positive child could be established in all cases of erythroblastosis.

Iso-immunization and consequent incompatibility as a result of transfusions were demonstrated by post-transfusion shock and by fatal erythroblastosis in one case in a primipara, who had previously received transfusions of Rh-positive blood.

The authors propose the term of "created incompatibility" to differentiate the new concept from normal incompatibility. In materno-fetal iso-immunization, the incompatibility is created naturally, while the repeated transfusions confer an artificially created incompatibility.

The created incompatibility should be investigated in any post-transfusion shock, remembering that the red cells of the donor in the blood of the recipient may falsify the result of the reaction; it is advisable to repeat the test several days later.

In the treatment of the hemolytic diseases of the newly born infant, it is preferable to use Rh-negative blood because its red cells survive longer and have a better therapeutic effect, and it is imperative to discard blood sensitized to agglutinin Rh.

The authors are now studying the presence of maternal hemolysin and its curve during pregnancy because they think it possible to diagnose the Rh factor in the child during its intrauterine life.

Of 61 pregnancies studied, 35 ended with the birth of children having erythroblastosis, a percentage of 57.4 which offers considerable support to the new pathogenic concept of these diseases. There were 14 normal children: 3 were Rh negative and 11 Rh positive. With the exception of two, the latter were children of primiparas supporting the theory that iso-immunization is only started during

the first pregnancy, and has not yet produced a sufficient concentration of anti-Rh hemolysin to induce erythroblastosis. The same conclusion is reached by comparing the number of cases of erythroblastosis in primiparas and multiparas, 8.5 and 91.4, respectively.

In none of the 12 cases of abortion and of death in utero was it possible to demonstrate the intervention of the Rh factor. This favors the authors' thesis that iso-immunization and, with even more reason, the transplacental passage of the maternal agglutinin into the fetal circulation occurs mostly during the final stage of pregnancy and during labor.

On the basis of their experiences in various studies on placental permeability, the authors suggest a method to prevent hemolytic diseases in the newborn infants. In pregnancies with the probable prognosis of erythroblastosis, premature birth should be procured before the placental tissue reaches its maximal permeability, or, still more radically, cesarean section should be performed to avoid uterine contractions, and thus protect the child from the action of the anti-Rh hemoagglutinins of the maternal organism.

J. P. GREENHILL.

Coatz, A. S.: *Chronic Appendicitis and Pregnancy*, *Semana méd.* 51: 370, 1944.

In the opinion of Coatz, chronic appendicitis is an affliction which is frequently encountered in maternity services. The symptoms are identical with those in nonpregnant individuals. The diagnosis in pregnancy, however, is not always easy. The treatment during gestation should always be medical and should consist of proper diet, rest, applications of ice if necessary, and strict observation of the pregnancy. In the puerperium, an appendectomy should be performed in order to avoid a similar attack.

J. P. GREENHILL.

Toxemia

Sage, Earl C.: *The Care of the Parturient Woman in Relation to Neonatal Mortality*, *J. A. M. A.* 124: 339, 1944.

The author discusses birth trauma, asphyxia, prematurity and maternal complications in relation to neonatal mortality. With regard to fetal asphyxia, prevention is as important as treatment. A proper anesthetic and a trained anesthetist are essential. Maintenance of body heat is also essential. Control of prematurity is also important in reducing neonatal mortality. Maintenance of body temperature, proper nutrition of the infant, prevention of cyanotic attacks, and prevention of infection are essential in this respect. Improved obstetrics is the best way of combating trauma. The numerous maternal complications affecting neonatal mortality are mentioned and discussed.

WILLIAM BERMAN.

Dubrovsky, Ricardo, and Linzoain, Enrique A.: *Treatment of Pulmonary Embolism Complicating Puerperal Thrombophlebitis*, *Semana méd.* 51: 64-66, 1944.

The authors state that pulmonary embolism results in exaggeration of vasoconstrictor, respiratory and cardiac reflexes and treatment is directed toward blocking these reflexes and dilating blood vessels. Morphine is used for the former, and papaverine in large doses intravenously for the latter.

Treatment is individualized according to the severity of signs and symptoms. In the presence of severe symptoms, 2 to 7 c.c. of a solution containing 0.03 Gm. of papaverine hydrochloride per cubic centimeter is injected slowly into the vein.

Simultaneously 0.01 to 0.015 Gm. of morphine hydrochloride is injected intramuscularly. In extreme instances, the morphine may be administered intravenously in a different vein from that being used for papaverine injection. In cases of lesser intensity, the papaverine is injected slowly and in the above dosage, but the least possible quantity of morphine (0.005 Gm.) is given, to avoid excessive depression of the respiratory center. In the mildest cases, 0.02 to 0.04 Gm. of papaverine is given intravenously without morphine. These dosages are rigidly followed, but varied according to individual indications. The highest dose of papaverine used by the authors was 0.20 Gm. on one occasion. Other authors have reported using even higher doses, but they have not found this necessary.

In most cases, even those with most severe symptoms, a favorable effect is produced by intravenous injection. As soon as vasodilatation occurs, the symptoms cease, the patient shows improvement and the injection can be stopped. Symptoms may recur with less intensity after several hours, when the injection is repeated. Even when symptoms do not recur, a second injection may be given as an adjuvant in the treatment of the pulmonary infarct which follows. A space of four hours has been arbitrarily set by some, but the authors believe the second dose should be administered according to the individual requirements of the patient.

Treatment of postembolic pulmonary infarct is similar to that for any acute pulmonary disease. Rest must be complete and prolonged and proper use of sulfonamides may prevent development of later sequelae. Inhalations of carbon dioxide are contraindicated unless too high dosage of morphine has depressed the respiratory center. Oxygen inhalations are valuable in treatment.

J. P. GREENHILL.

Ferreira, Jorge, Cid.: Early Rising After Delivery and the Service of Obstetric Assistance in the Home, Rev. de ginec. e d'obst. 37: 288-291, 1943.

The author states that the two are interdependent. Mother and child are sent home from the hospital between the third and seventh days and there they are attended and followed up by the service until complete recovery.

To be allowed up early, primiparas and multiparas must fulfill the following conditions: normal birth without traumatic or surgical lacerations, axillary temperature not over 36.8° C., normal lochia, firm uterine involution under 11 cm. from the pubic symphysis, normal urinary and digestive functions, regular milk function and good general condition. About 1 in 10 usually fulfill these conditions. Besides being beneficial, early rising increases the useful output of each maternity bed.

J. P. GREENHILL.

Da Costa, Luiz Alfredo Corrêa: Revision of Uterine Cavity as Prophylaxis Against Puerperal Infection, Rev. de ginec. e d'obst. 37: 295-300, 1943.

The author has used the method of Gheorghiu in 54 cases: 36 normal labors and deliveries except for retention of membranes, 5 normal labors followed by hemorrhage and manual extraction of placenta, 9 surgical births with retention of membranes and 4 surgical births with hemorrhage and manual extraction of placenta.

In the group of 36 cases, puerperal infection occurred in 2.7 per cent. Puerperal infection was listed when the temperature reached at least 38° C. twice in 24 hours.

In the other 18 cases, there were six infections; however, they occurred in severely ill cases: fever during labor in two, vaginal tamponing in two (one with perforation of uterus), forced dilatation with rupture of cervix in one and version after various trials of forceps in one.

There were no deaths, but the limited number of cases does not allow general conclusions.

The interesting cases are those of revision for simple retention of fragments of membrane, with an infection rate of 2.7 per cent which could even be reduced. In 100 similar cases under expectant observation sometimes helped by small doses of oxytocics, the incidence of puerperal infection was 8 per cent. Consequently, it is advantageous to revise the uterine cavity after birth when the membranes are not completely expelled, or when there is doubt about the integrity of the placenta.

Gheorghiu's method is as follows: The patient is anesthetized with ethyl chloride and, using all aseptic and antiseptic precautions the hand is introduced one or several times into the uterine cavity until it is completely cleaned of any remnants of membrane. Then the uterine cavity is washed with boiled water, using a Budin No. 30 sound and aiming only at a slight mechanical cleansing effect. The current of water must have low pressure and be stopped before the sound is removed, so that all water runs out first. The vagina is also washed out under low pressure. With this method, the morbidity rate in the author's clinic has fallen from 20 to 25 per cent in 1913, to 2 to 3 per cent at present.

J. P. GREENHILL.

Vaginal Infections

Dubois, P.: *An Effective Treatment of Trichomonas Vaginalis Vaginitis*, Schweiz. med. Wchnschr. 74: 1944, 1944.

The trichomonas vaginalis belongs to the family of protozoal parasites in man and certain ones such as *Plasmodium malariae* and *Lambliia intestinalis* can be destroyed by quinine. By analogy, Dubois of the Lausanne Woman's Clinic reasoned trichomonas vaginitis should respond to quinine. He therefore experimented with many chemical agents and drugs, and found that in reality, quinine immobilized *Trichomonas vaginalis* more quickly than the other agents he employed. He therefore prepared vaginal suppositories containing quinine and used them in 25 women who had trichomonas vaginalis vaginitis. Only 10 women returned for regular treatments but the results were good. Relief was obtained after the use of two suppositories daily for 8 to 10 days.

J. P. GREENHILL.

Coutts, W. E., Brieva, J., Lerner, J., and Said R.: *Virus Infections of the Vulva, Vagina and Uterine Cervix*, Obst. y ginec. latino-am. 2: 9-21, 1944.

The authors examined a large series of prostitutes in Santiago, Chile, and found a number who had virus infection. A characteristic of such infections may be found in material obtained by biopsy. This consists of the presence of inclusion bodies found in the cytoplasm or nucleus, or in both, and their presence also in the intercellular spaces. Special staining methods have enabled the authors to study the chemical composition of these inclusion bodies and to make the correct diagnosis.

J. P. GREENHILL.

Rieper, J. P.: *Treatment of Trichomonas Vaginalis Vaginitis*, An. brasil. de ginec. 8: 257-267, 1943.

The author reports a series of 16 women treated for trichomonas vaginalis vaginitis by means of negatol. In this series 81 per cent were cured clinically but only 37.5 per cent were freed of the trichomonas organisms. Negatol produces a superficial necrosis which sterilizes the vagina, but reinfection takes

place because of secondary foci and primary sources of infection, and this is the main problem in the treatment.

J. P. GREENHILL.

Dos Santos, A. F., and Zagury, S.: *Trichomonas Vaginalis* and Its Treatment, *An. brasil. de ginec.* 8: 167-178, 1943.

The authors treat *trichomonas vaginalis* vaginitis by means of sulfonamide suppositories. Of 39 women treated by this means, 30 were cured and 9 discontinued the treatment. In 55.5 per cent of the cases, examination of the husband's urethra revealed the presence of *Trichomonas vaginalis*. This is the source of reinfection according to many authors. The organism was also found in the urethra of 33.3 per cent of the patients. No organisms were found in the rectum.

J. P. GREENHILL.

O'Sullivan, J. V., and Bourne, L. B.: Supervision of Pregnant Women in Factory Employment, *Brit. M. J.* 4333: 108, 1944.

The authors describe the British System of caring for pregnant women working in factories. Factory antenatal clinics are advised. Under medical supervision it was found that many women can do suitable work to an advanced stage of pregnancy. Nursing mothers were not advised to recommence work until at least three months after delivery, and day nurseries must be established if a return to work becomes necessary.

WILLIAM BERMAN.

Dutra, Licinio H.: Sulfonamide Therapy in Gynecology and Obstetrics, *Rev. de ginec. e d'obst.* 37: 277-287, 1943.

The author finds that the use of sulfonamides is obligatory in the prophylaxis and treatment of puerperal infection. Thus, any woman who had a prolonged delivery, premature rupture of the membranes, several vaginal examinations, assistance by nonprofessionals or an obstetrical intervention must be given sulfonamides. Whenever possible, their use should be started before the end of labor in doses of 4 to 5 Gm. daily, and after labor, oxytocics and blood transfusions should be administered, if necessary. The slight elimination of the drugs in the milk (2 to 6 centigrams in 24 hours) does not contraindicate breast feeding.

According to Speert, intravenous injection of sodium sulfathiazole or sodium sulfadiazine must be used in intercurrent or intrauterine infection during labor, or in cases of gonorrhea of the mother to protect the child.

Various sulfonamides have been successively used in the treatment of gonorrhea. Recent work by Douglas, Davis and Shandorf shows that sulfathiazole and sulfadiazine are more specific and rapid and much less toxic than sulfanilamide, and that sulfadiazine seems to be more efficient. Bacteriologic cure is frequently observed between 9 and 12 hours after the use of sulfadiazine and sulfathiazole, while sulfanilamide takes 40 to 50 hours to give the same result. The ideal form of treatment would consist of 4 Gm. of sulfadiazine or sulfathiazole daily for six consecutive days. These facts are being confirmed by the literature.

In gonococcic vulvovaginitis of infants the author has obtained much better results with estrogen therapy than with sulfanilamide or sulfathiazole.

The indications for the intraperitoneal use of sulfanilamide in powder are: peritonitis caused by bacteria or gastrointestinal contents; contamination of the sterile peritoneal cavity by opening of an infected cavity; a drained abscess cavity (Douglas); to avoid formation of adhesions in nonperitonized areas and in me-

chanical or chemical irritation; in exposure of the endometrium in the course of conservative myomectomy or hysterectomy; in cases of cesarean section performed in the presence of fever or old ruptured membranes.

Extraperitoneal indications for the use of sulfanilamide powder are abscessed or exudating cavities opened surgically (abscess of Bartholin's gland), incomplete and infected abortion without suppuration, impure forceps and version cases, vaginal and cervical laceration, uterine prolapse and other plastic operations of the lower genital tract and vaginal discharge due to trichomonas.

J. P. GREENHILL.

Kirchoff, A. C., Racely, C. A., Wilson, W. M., and David, N. A.: An Ergonovine-Like Oxytocic Synthesized From Lysergic Acid, *West. J. Surg.* 52: 197, 1944.

Addition of hydroxybutyl amide 2 to lysergic acid produces a compound that structurally resembles ergonovine, and produces a motor effect upon the uterus in every way similar to ergonovine. Tested on excised muscle strips of the guinea pig, rat, dog, and rabbit uterus it gave in comparable dosage, a motor reaction in every way comparable to ergonovine. Studies on the human being revealed an increased tone and motor response after a 3-minim dose by mouth in a woman near term. In 26 cases the drug was given in a dose of 0.2 mg. intravenously as the anterior shoulder was being delivered. The placenta was delivered in an average of 3.2 minutes and the reaction of the uterus in every way paralleled the response following comparable doses of ergonovine. There is a slight rise in blood pressure following the administration of M.E. 277 (Methergine), but apparently no sympathicolytic action because it failed to inhibit the epinephrine blood pressure rise in dogs and the epinephrine motor response in the rabbit uterus.

The synthetic preparation of such a product is important because of the limited ergot supply, and the difficulties found in obtaining potent raw material even where crude ergot is obtainable.

WILLIAM BICKERS.

Leon, Juan: *Obstetric and Obstetric-Gynecologic Specialization*, *Semana méd.* 2: 667, 1943.

The author comments on the controversy as to whether obstetric and gynecologic practice should be separated or combined. He points out that the essential function of the genital apparatus is reproduction. Gynecologic diseases are intimately concerned with the reproductive function; hence logically, study of physiology and pathology of the same organs cannot be separated. It is not necessary that a physician trained in obstetrics and gynecology should practice both specialties, but he will be better prepared to function as either type of specialist. In any case, however, specialization is indispensable.

A training program of six years is proposed. This is considered the minimum necessary to acquire in an orderly, disciplined form, the clinical experience necessary for practicing obstetrics. Specialization in obstetrics and gynecology simultaneously requires more time, at least ten years.

The suggested program comprises three cycles of two years each. The first period has for its object the general study of gynecology and everything pertaining to the physiology of pregnancy, parturition, the puerperium, and the newborn infant. The second period is devoted to the study of the pathology of pregnancy, parturition, the puerperium and the newborn infant. The third period covers the whole field of obstetrics. The candidate during the first two periods should serve as second assistant in the clinic, and in the consulting rooms, and should gain surgical experience as second assistant, first at simple operations and normal de-

liveries, and later in more complicated cases. During the third period, he should function as first assistant both in the clinic and the operating room, and should have first-hand experience in all types of pathologic and septic conditions.

J. P. GREENHILL.

Brenner, F. T.: A New Breech Forceps, Am. J. Surg. 55: 181, 1942.

A new type of forceps is described in which the handles meet the blades at an angle of almost 45 degrees. The blades are of the fenestrated Elliott type, and the handles fit together with a swivel action, being locked by a thumb set. The forceps are applied to the aftercoming head in breech deliveries over the shoulders instead of under, and extraction is accomplished by exerting pressure upward and over the mother's abdomen with a circular motion.

FRANK SPIELMAN.

State, D., and Levine, M.: Human Plasma and Serum Toxicity, J. Lab. & Clin. Med. 28: 1786, 1943.

That reactions occur in the course of serum transfusions has long been known. However, references to plasma reactions are meager so that it has been assumed that they do not take place. During the administration of several thousand plasma transfusions at the University of Minnesota Hospitals, the authors observed that reactions were not infrequent. In order to determine the factors involved in causation, they investigated the group specific plasmas by skin test especially with regard to the A and B substances. Sensitivity could be demonstrated to either, or to mixtures of A and B in individuals who developed reactions from their use. The conclusion reached was that plasma pooling is not a sure method of preventing reactions due to these substances. When the A and B factors are not involved, the following may also cause disturbances: 1. The presence of allergins in the plasma or serum. 2. The presence of reagins in the plasma or serum. 3. The presence of pyrogens. 4. The presence of immunologic factors as yet unknown. The authors conclude that skin test using the specific plasma to be transfused is a good method of indicating sensitivity in many cases and an aid in preventing transfusion reactions.

FRANK SPIELMAN.

Items

American Board of Obstetrics and Gynecology

Examinations

The general oral and pathology examinations (Part II) for all candidates will be conducted at Atlantic City, New Jersey, by the entire Board from Thursday, June 14, through Tuesday, June 19, 1945. The Hotel Shelburne in Atlantic City will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel.

Candidates for re-examination in Part II must make written application to the Secretary's Office not later than April 15, 1945.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

Deferment without time penalty under a waiver of our published regulations applying to civilian candidates, will be granted if a candidate in Service finds it impossible to proceed with the examinations of the Board.

Applications are now being received for the 1946 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

Necrology

WILLIAM LATZKO, M.D., obstetrician and gynecologist, former professor at the University of Vienna and chief of the department at the Kaiserin Elizabeth Hospital in that city, died in New York after a prolonged illness, at the age of 81, on Feb. 11, 1945. A pioneer in the treatment of osteomalacia with phosphorus, a leader in the development of female urology as a part of gynecologic practice, universally known for the operation of extraperitoneal cesarean section named for him, the author of many contributions to the literature, he left Vienna in 1938 and practiced in Buenos Aires for several years before coming to this country where he remained active until his death.



Frank Worthington Lynch
1871-1945

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In Memoriam

FRANK WORTHINGTON LYNCH, A.B., M.D.
1871-1945

Dr. Frank Worthington Lynch, a member of the Advisory Editorial Staff of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY since its founding, died on Jan. 12, 1945, of cardiac failure. He is survived by his wife, Rowena, and a son, Frank W. Lynch, Jr.

Dr. Lynch, son of Frank W. and Rebecca Nevin Lynch, was born in Cleveland, Ohio, Nov. 5, 1871, graduated from the Western Reserve University with the degree of A.B., in 1895. He received his medical degree from Johns Hopkins (1899) where he served as house officer and associate in obstetrics under J. Whitridge Williams from 1900 to 1904. Postgraduate study in Vienna and Munich for several years preceded his location in Chicago where he held the position of Assistant Professor in Obstetrics and Gynecology in Rush Medical College (University of Chicago) from 1909 to 1915. He became Professor of Obstetrics and Gynecology in the University of California Medical School (1915 to 1942) and then Professor Emeritus from 1942 until the time of his death.

Dr. Lynch was greatly interested in medical education, hospital standardization, and maternal welfare, but his major contribution to medical progress was his method of treating carcinoma of the uterine cervix. Dissatisfied with the often inconsistent and unpredictable results which followed radium treatment of early and apparently curable cases of cervical carcinoma, he was convinced that a more favorable outcome could be obtained by combining the advantages of radium and the radical surgical removal of the growth. His meticulous records of family history, photomicrographs, careful and frequent patient check-ups, autopsy reports, and 100 per cent follow-up studies served as a model for every cancer clinic in the country and offered convincing evidence of the wisdom of his method of treatment.

Membership in scientific societies included American Gynecological Society (President, 1933); Fellow American College Surgeons (Vice-President, 1937); Fellow American Medical Association (Chairman of section of Obstetrics and Gynecology, 1924); a founder and first President of Pacific Coast Obstetrics and Gynecologic Society, 1931; Pacific Coast Surgical Society, and numerous honorary memberships in Pacific States medical societies.

Dr. Lynch's extensive clinical experience furnished informative material for many medical publications in American and German literature. He contributed chapters to *American Practice of Surgery*, 1911; *Oxford Surgery*, 1921; *Monograph on Pelvic Neoplasms*, 1922; *Nelson's Loose-Leaf Surgery*, 1928; *Davis' Obstetrics and Gynecology*, 1933; and *Curtis' Obstetrics and Gynecology*, 1933.

Eight years ago, Dr. Lynch had his first attack of coronary occlusion, which necessitated bed rest for many months. When he became ambulatory he resumed his activities, nor did the warning of his medical advisers and many subsequent attacks of cardiac weakness prevent him from giving himself enthusiastically and unstintingly to medical service. He wanted his end to come quickly, while he was active and useful; fortunately his wish was granted. Though he has passed from this life, his attainments, courage, and cheerfulness will not be forgotten.

ALICE F. MAXWELL, M.D.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons

Fifty-Sixth Annual Meeting, Hot Springs, Va.

September 7 to 9, 1944

PRESIDENTIAL ADDRESS

THE DIFFERENTIAL PSYCHOLOGY OF THE AMERICAN WOMAN*

WILLARD R. COOKE, M.D., GALVESTON, TEXAS

IN THE practice and in the literature of gynecies, very little attention is paid to a factor which, insofar as the subjective welfare of the patient is concerned, is more important than the mere correction of physical and functional pathologic states. Ninety-five per cent of the severity of human suffering is mental; a great deal of the symptomatology encountered in the practice of gynecies is of purely mental origin. Therefore, if we are to relieve the major part of our patients' suffering, we must do so through psychotherapy, and successful psychotherapy must be based upon an understanding of the patient's mental processes. Up to a certain point, the mental processes of man and woman are alike, but beyond this point there is divergence to an ultimately extreme degree. In women, far more than in men, ideation and mental activities are dominated by the reproductive factor and its side issues. Reproduction is the central physiologic *raison d'être* of woman, marriage is normally her goal and lifework, and the disappointments and annoyances of the menstrual and reproductive cycles keep her constantly reminded of the necessity for planning all of her activities in relation to this basis.

These facts are well known. The motif of this address is an attempt to rationalize some of the less well understood peculiarities of female psychology. In a sense this discussion will be academic in that no correlation of the basic psychology with clinical entities will be included. The ideation and phraseology will doubtless be subject to criticism, since they represent merely the observations made during thirty years of the practice of gynecies by one unlearned in the concepts and terminology of modern psychiatry.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Throughout, the psychologic elements common to both sexes will be largely disregarded. Since these common elements comprise most of the human virtues, this discussion may seem unduly critical and will certainly be regarded as a personal diatribe by almost every woman who may read it, yet no one more than I recognizes and appreciates the superiority of women to men in many directions. No reference will be made to such factors as narcissism, masochism, passivity, identification, etc., important as these may be to a complete understanding of the problem.

It is unnecessary to point out to the Fellows of the Association that this discussion is concerned with the fundamental bases for such peculiarities of ideation and action as are encountered by the obstetrician-gynecologist in the study of his patients. The majority of patients, especially in cases of functional disorder, are sooner or later likely to present some psychologic element causing, arising from, or modifying their physiologically expressed disturbances. The gynecologist is also likely to be made a sort of father-confessor to a large number of his patients and his advice sought concerning the patient's personal problems. In considering these problems, it should be remembered that there is a quite definite relation between the psychologic processes and the social-financial status of the individual. Idleness, although earnestly sought after by most women, is a definite pathogenic factor in their lives. One rarely encounters a patient in the upper-income groups who does not suffer from some form of psychoneurosis directly traceable to: first, mental and physical stagnation resulting from lack of occupational and recreational resources; or second, a cultivated egocentrism or its frustration, according to whether the wife or the husband is the dominant partner—and in these groups the dominant husband is a rarity. Such disturbances are rarest among women who must work to contribute to the family's support and next among housewives who do their own work and are content with this destiny (although in the lower-income group the husband is frequently dominant and likely to be indifferent to the psychologic necessities of the wife).

The Basic Psychosexual Status of Woman

The basic psychosexual status or instinct of woman is tripartite: first, the urge to reproduce the species—the second law of nature; second, pregnophobia; and third, the maternal instinct. The second is in direct opposition to the first and last; hence the cornerstone of female psychology is unstable in that there exists a constant factor of mental conflict. This conflict may, in some cases, be wholly in the subconscious, but pregnophobia, recognized or unrecognized, is a disturbing element in every married woman's life, and many women spend their entire reproductive married periods in a state of more or less severe anxiety psychoneurosis. That this conflict is fundamental is

evidenced by the fact that the female animal (strongly urged as she is by the second law of nature) never submits to coitus without a preliminary battle.

A secondary element must be taken into account: The hypersensitization of the nervous system which occurs during the premenstrual phase of the cycle. That this is a very potent factor in the psychology of woman is evidenced by the report of a Parisian prefect of police: that 84 per cent of all the crimes of violence committed by women are perpetrated during the premenstrual and early menstrual phases of the cycle. Alteration of personality during this stage is a matter of common observation, of tradition, and of history. At present, we must accept this phenomenon as a fact not satisfactorily explained upon a chemical or hormonal basis.

When a woman discovers or imagines that she is pregnant, several conflicting emotions come into play. On the one hand there is the subconscious satisfaction of the maternal instinct and, frequently, delight in the prospective advent of the baby. On the other hand there is the basic subconscious pregnophobia with its conscious exaggerations, fear of pain, fear of death, dislike of the inevitable deformity, and often hatred of the unwanted child and of its father. Given such a foundation of conflict, it is only natural that the horrors of which she has heard and of which she will certainly be plenteously informed by her female "friends" tend to create a psychoneurotic superstructure which is apparent in a great many cases. Tocophobia is probably responsible for most cases of motor dystocia. Fear of the unknown in labor seems to be the origin of most of the inhibitions of motor function and of the exaggeration of pain, and, in fact, constitutes the real difference between the primigravida and the multigravida in labor.

Finally, there is one phase of woman's life in which psychoneuroses play a definite and all but universal part: that is, the climacteric. Whether or not hormonal imbalances are per se responsible for symptoms, it is certain that the major severity of these symptoms is due to psychologic magnification. Idiots and men almost never present any evidence of severe symptoms, Negroes rarely. The basis for these symptoms, or for their magnification, lies in three more or less universal misconceptions. The woman has had the terrors of the "change of life" forced upon her from girlhood by other women; she almost always believes that with the menopause her sex life will end; she feels that after the climacteric she will be an old woman, wholly unattractive in any way. The falsity of all of these ideas is obvious. Proper psychotherapy will do more to prevent or relieve the symptoms of the climacteric than all other forms of treatment combined, and it seems probable that most other forms of treatment are effective chiefly through their psychotherapeutic effect.

The Mental Conditioning of the Female Child

Throughout the history of civilization there has been a trend toward the shielding and idealization of woman. On the part of the male this protection has been founded upon male jealousy and upon the desire to preserve the mental and physical beauty of the adored female; on the part of mothers and women in general, it has been carefully inculcated and nurtured in the male child in order to ensure for themselves a mode of life as free as possible from drudgery, responsibility, and other unpleasant experiences. In the modern family, this attitude is likely to be carried to an extreme—in America, to an extent which has become ridiculous and deleterious to the welfare of the female child. From babyhood, when economic circumstances permit, the majority of girls are waited upon hand and foot, their whims are humored and even encouraged, and they are subjected to the psychic trauma of incessant admiration and flattery. The higher the level of "society," the worse the damaging imprint upon the girl's mind is likely to be. A very wise woman has said that she has never known any woman to be completely happy who had not been obliged to do her share of the family's work as a child and to work for her own living during early maturity and after marriage. The total egocentrism and unwillingness to work of most of the daughters of well-to-do families and their inability to carry out the simplest duties in a satisfactory way have been amply demonstrated during the present emergency.

Woman in Relation to Herself

Since woman is primarily a reproductive organism, the frustration of this essential leads to protean physiologic and psychologic aberrations, especially after the age of 30 years. Part of this frustration is purely physiologic, but the major part is a psychologic reaction to a conscious or subconscious sense of failure or inferiority. Exceptions to this rule, of course, are fairly frequent, chiefly in the rather commonly occurring wholly asexual individuals who have never felt the urge toward marriage and therefore experience no frustration. The winning of a husband is the principal occupation of the average woman. She is trained to it during adolescence, and almost all of her social life and contacts are designed with this end in mind. Hence, there is an intense concentration on the development of personal beauty, adornment, and attractiveness to a degree which reacts to create a dominant egocentrism. This egocentrism is still further nurtured by social techniques, of which the debutante system is the most exaggerated. Only the very exceptional woman can be satisfied with an ordinary life with her feet on the ground after having been catered to as a goddess during a year or more of the formative period of her life. The average woman who has not had to make her own living or to do her own household work during her adolescence and early

maturity is almost certain to regard her own interests as paramount and to resent and to suppress anything which conflicts. Almost every act of the unmarried woman's life is gauged primarily by "how will this affect ME?" or by "what impression in regard to ME will this make?" This attitude is often reduced in the case of the happily married woman but far too often persists to make the activities of everyone with whom the woman is connected subordinate to it. In the development of the urge to be more attractive than other women, a curious mixture of orthodoxy and individualism develops. If it is fashionable to wear many layers of clothes which hamper every movement and accessories which cause acute pain, the woman will wear such things; if it is fashionable to go naked, she will go naked. In either case, however, she will add a touch of her own which will set her apart to some extent above the herd. The planning of such touches in such a way that they may be individual and yet not transgress the great law of fashion occupies a great deal of a woman's time and gives rise to a great deal of anxiety, fear, and disappointment, especially in socially ambitious women of limited income. The cycles of fashion probably depend upon the desire or psychologic necessity for standing out distinctively on the part of women who feel that the opinion of other women need not be considered—courtesans on the one hand, actresses and established social tyrants on the other. Having its origin in the fundamental desire to appeal to the male, the whole process of self-adornment has gone far astray from its natural goal. As a result of this concentration upon conformance to fashion and the desire to outshine other women, the average woman comes to feel that what she wants is an actual necessity. She will deprive herself and her family of pleasures, of food, of comfort, and of happiness in order to maintain the superiority of the appearance of herself and of her home.

Woman in Relation to Her Mother

That this relationship is a great factor in the psychology of woman can be testified to by any obstetrician. In general, there are three more or less normal types of mother (excluding the definitely pathologic groups): First, and worst, there is the mother who sublimates herself in the daughter, waiting upon her hand and foot, depriving herself of pleasures and even of necessities in order that the daughter may have every advantage and no unpleasant experiences. The daughter of this type is unable to perform even the simplest personal and domestic tasks—mother has always done everything for her. Minor or major disaster always results when (usually after years of frustration in trying to discover a man who can meet the mother's requirements) such a daughter is thrust into constant association with a man accustomed to the self-dependency, the give and take, and the teamwork of male life. Pregnophobia is all but universal in such cases. The psychologic anguish and terror of such a woman confronted by

labor, when she discovers that neither her husband nor her mother can have her baby for her, is pitiable. Motor dystocia, cesarean section, disastrous operative deliveries, and permanent psychoneuroses are all too common in such cases, but the obstetrician's contempt should be reserved for the mother, not the daughter. The second type of mother is fortunately still predominant in numbers, although it does seem that they are being reduced, generation by generation (possibly as a result of higher average incomes). This type of mother, through common sense or necessity, follows the natural law of teaching the fledgling to fly and then making it dependent on itself. The daughters of such mothers, particularly if they have been obliged to make or contribute to their own living, are by far our most psychologically stable women. A heartening reaction on the part of the women themselves has recently become apparent in the rebellion of girls and young women against the Victorian dicta which removed from any social standing the woman who dared engage in useful or profitable activities outside the home. The third type of mother forms the smallest group, although far too common and apparently increasing in numbers. This type is not a mother at all: her total egocentrism ejects her unwanted child from her life at the earliest feasible moment. The daughters of these mothers present a high percentage of psychologic variants of all types and furnish a very troublesome proportion of the psychiatric problems to be solved by the medical profession.

Women in Relation to Men Before Marriage

The instinctive urge to be attractive to the male appears very early in life, as is evidenced by the popularity of kissing games and by the frequent seeking of physical contact and caresses by very young girls. Instances of seduction to phallic contact are by no means rare. Later, as the little girl is taught the taboos, fear of parental opinion restrains these premature urges, and, in the prepubertal period, an artificial indifference normally becomes dominant. In some individuals a sense of inferiority to the male sex makes its appearance, and many psychoneuroses may be founded upon this basis. During the period of adolescence and early maturity, the early indifference becomes tempered in varying degrees by a confused germination of the maternal-reproductive-sexual instinct modified by the amplified taboos of civilization. In most cases, this awakening is in the direction of a desire to be admired and sought after by boys in general. Sooner or later a reactive selection of individuals to be especially attracted is made until, in the average case, the field is narrowed to the individual. In this process, of course, the attitude and activities of the boy or young man play a considerable part. During the early stages the girl is likely to feel the attractiveness of the male in the form of an idealization in which actual sexual desire is not recognized—this is best instanced by the adoration of actors and other heroic figures. When the field is

narrowed to the individual, the complex emotion of love may enter the picture. This emotion is too variable and too complex to be defined, yet it may be broken down into certain basic varieties.

First, there is love in its supreme manifestation as the permanent and indissoluble merger of one personality into another. This, while the most beautiful of all human relations, is very rare and to most people so incomprehensible that its existence is denied. That it does exist is best evidenced by the case of the wife who cleaves to the brutal and criminal husband, returning with unchanged devotion and loyalty to him after his release from years in prison, or by the case of the husband who sacrifices all of the pleasures and interests of his own lifetime to the fulfillment of every demand and whim of a totalitarian dictator or a whining psychoneurotic pseudo invalid. Such love is probably nonexistent in the absence of a strong sexual element, yet this fundamental desire is wholly subordinated to spiritual affection, arising only as a secondary reaction and climax to an upsurge of the more ethereal emotion. A similar relationship is possible in the absence of the sexual element but must then be designated as supreme friendship rather than love. Such a relation is common between men, forms the basis of some successful marriages, is possible between man and woman (although this possibility is denied almost universally by women), and is probably impossible between woman and woman if both conform to the general pattern.

The second degree of love is the so-called "puppy-love," which is an element in nearly every youngster's life. It is identical with true love except that it is temporary. While it lasts it is a beautiful emotion and one not to be ridiculed. Curiously, very few illegitimate pregnancies originate in cases of this sort, largely because of the attitude of the boy involved. A man truly in love is likely, consciously or unconsciously, to subjugate the sexual instinct as much as possible because he feels that it is a profanation; on the other hand, the woman in love is likely to become totally amoral as regards her loved one. In most instances where pregnancy has occurred in such cases, the girl or woman will admit that the seduction was on her part. Of course, a great many illegitimate pregnancies result from an unscrupulous man's taking advantage of a girl who is or thinks she is in love with him. As a digression, it may be noted that in the majority of cases of ordinary illegitimate pregnancy in girls from the intelligent classes the girls admit that they were not in love, that they were fully aware of the dangers connected with coitus, that they felt neither desire for nor pleasure in the act, and that they yielded simply because "he had been nice to me and I felt that I ought to do what I could to be nice to him." The "victory girl" is one extreme example of this ideation, which is apparently the ultimate expression of the generalized as opposed to the individualized intersexual relationship.

A third degree of love is the most common of all types and the basis of most successful marriages. Founded originally on liking, respect, and gradually established confidence, the marriage is consummated while the sexual element is very weak or entirely lacking in the woman. As many women put it, "I was in love with love without having any idea what love was." One of the most disastrous of emotional disruptions occurs in the case of a partner in such a marriage who later experiences the development of a higher type of love toward another individual. An amazingly large number of marriages have no foundation in any degree of love on the part of the wife; by their own admission such women marry solely for economic reasons or to eradicate a specific or general sense of failure. Marriage is the business of woman; no one likes to fail in business, and no woman likes to feel that other women have been more successfully attractive than she herself. In contrast, the average boy or unmarried man is not likely to think of marrying (except occasionally in a vague way as something that most men do) until they either fall in love or decide to marry for financial or other reasons. When they do think of it, it is usually with a sense of fear or aversion in the light of the great limitations placed upon independence and the mode of life which they have observed in other men after marriage. Men are therefore, more than women, likely to marry under the compulsion of some sort of love; and this love is inspired by and directed toward a single individual. With most women, the ingrained idea of marriage as a business leads them to consider many men as possible husbands, and it is not unusual for a woman who later becomes an ideal and constant wife to be uncertain up to the last minute which of several suitors she will select (or even to change her mind after the selection has been made). Even when the woman is truly in love, her mental attitude is still colored by her lifelong habit of thinking in the direction of marriage. The mental attitude of the suitor and young husband in love is one of worship, complete self-forgetfulness, and the desire to please. The mental attitude of the bride is likely to be chiefly egocentric, tinged with some uncertainty as to the wisdom of her choice and with a more or less vague fundamentally pregnophobic fear of the male who is about to invade her life.

Quoting from a verse by an unknown author appearing in the *Journal of the American Medical Association*:

When a man asks a maid and she says she'll be his,
He hopes she'll forever remain as she is.
When a maid has said "Yes," she commences to plan
For complete alterations to make in her man.
A maid to a man is a vision ethereal;
A man to a maid is a piece of material.

The question often arises as to the factors which make a man attractive to a woman. From analysis of the testimony of a good many

women, it appears that the prime factor lies in his spontaneous fulfillment of the egocentric necessities of the woman; that is, in his admiration (if not too clumsily expressed) and spontaneous forethought in catering to the woman's comfort and her need for personal flattery. A physically repulsive man may become a feminine idol through remembering such little things as the woman's preferences in food, flowers, and amusements, the details of his previous contacts and conversations with her, anniversaries of special occasions, and similar items which indicate to her that she occupies a prominent position in his thoughts. On the other hand, the fascination which many women feel toward the man who is indifferent or brutal to and contemptuous of women is a very common phenomenon. It is due to two factors in variable combinations: first, to the instinctive primitive female desire for male compulsion; and second, to the challenge to her own ability to fascinate the male. Physical beauty in men has very little appeal for women, facial beauty an appeal only in the idealistic sense. On the other hand, care in the details and appropriateness of clothing and personal appearance is of great import to most women. To some degree, this constitutes a tendency toward fetishism, which may be the source of serious marital difficulties. It is biologically natural that the male libido is easily excited by any simple sensory contact (such as the visual or tactile) with the female; it is equally natural that the excitement of the female libido is a complex and indirect phenomenon based upon the overcoming of sex fear and of the artificial impediments of civilization.

Woman in Relation to Her Husband

Sooner or later the subject of "husband trouble" crops up as a problem in a great many cases of gynecic functional disturbance. While this is essentially of psychologic origin and nature, and therefore in the field of the psychiatrist, the psychiatrist rarely has the opportunity to deal with the problem until it is far advanced and frequently incurable. The gynecologist, on the other hand, is in a position to perform an invaluable function in the field of preventive medicine, since his contact with the problem is early. Proper explanation at this stage often averts marital disaster, always provided, of course, that the patient is intelligent enough to understand and is willing to cooperate to the extent of some suppression of her egocentric instinct. (The marital problems of dyspareunia, frigidity, and impotence are outside the scope of this address although definitely and essentially germane to the subject.) Some part of "husband trouble" stems from ignorance on both sides of the essential differences in sexual appetite between the sexes and can be quite easily explained away. Biologically, the male is put into the world to fertilize as many females as possible and is therefore endowed with easily aroused and almost infinite capacity for coitus. This is a simple and direct instinct. The

female, however, knows instinctively that coitus is an intensely individual problem involving great future suffering and responsibility. The conflict between the second law of nature and pregnophobia inhibits her libido reaction, and a prolonged period of graduated sex play is necessary to the elimination of these inhibitions. As a final touch, the female welcomes the properly timed compulsion of the male which relieves her of responsibility. In many women, this final compulsion is the strongest of all the stimuli to a satisfactory reaction. Many marital difficulties, of course, are directly the fault of an inconsiderate, indifferent, domineering, brutal, or amoral husband. On the other hand, it is startling to discover through the wife's own admissions that the majority of the cases of "husband trouble" can be traced directly to female peculiarities of behavior which cause in the husband the reactions complained of by the wife as being original defects in *his* character or behavior. These cases should be classified as "wife trouble," although husbands very rarely seek medical help in the solution of the problems presented to their uninformed and amazed minds. In such cases, a careful ratiocination of the attitudes of both husband and wife and a step-by-step explanation of why the husband rebels and finally reacts against certain conditions of his family life will solve the problem and (again if the wife can and will suppress her egocentrism) avert disaster.

Wives, within the normal psychologic ranges, may be grouped as follows: The average wife, after a time during which the wishes of the husband are considered in regard to household affairs and arrangements, begins to shift furniture about and to purchase small items of unnecessary household equipment or decor. The first marital unpleasantness is apt to arise when the husband comes home and finds that his smoking table has been replaced by an impracticable gadget covered with trash and that his favorite chair now occupies a poorly lighted new position. From such small beginnings, the average wife goes on to an irritating shifting-about of all the husband's possessions, to throwing away his treasures on the excuse of their being shabby or old, to irritating dictation in regard to his dress and appearance, and to the purchase of household and personal items whose cost exceeds the husband's ability to pay. The wife, who at first insisted on sharing her husband's recreations, begins after a while to make these recreations unpleasant until they are abandoned. For example, she loyally goes fishing with him for a year or two and then begins to complain of cold, wet, mud, fish slime, mussed clothes, inadequate toilet facilities, interference with her own chosen activities, etc., until he gives up his fishing in despair. Most couples finally arrive at some reasonable compromise: the husband accepts his new life philosophically because the old habits are not worth the cost in argument, vituperation, sulking, and tears, and all is well. On the other hand, many

a wife, realizing the tremendous power which marriage and the male dislike of squabbling gives her, begins to assume more and more dominance over not only her own and mutual affairs, but also over all of the husband's activities. The comic strips of the daily press constitute a remarkable document of marital life in present-day America. A few of these strips indicate a very high order of intelligent observation and might well be made "required reading" in courses on gynecies.

The dominant wife begins to criticise her husband's clothes, friends, independent recreational activities, and business life (she is apt to be wise enough to leave his business methods alone). The husband's choice of clothing is denied, some or all of his friends are frozen out, he must cease any recreation in which his wife does not share, he must be ready regardless of disinclination or fatigue to share in the nocturnal social activities of his wife, and by degrees he becomes deprived of any volition outside the direct conduct of his business. The least rebellion excites in the dominant wife an emotional storm which is primarily an attack of rage engendered by the frustration of her necessity for domination, secondarily a weapon for the subjugation of the recalcitrant husband. Insofar as such a wife's well-being is concerned, there are only two solutions: the death or the total surrender of the husband. Separation and divorce constitute such a terrific frustration of the wife's necessity for domination that her psychoneurotic reactions are certain to become extreme.

The greedy wife asserts a dominance especially in the direction of the expenditure of income or more than income. Almost universally, if a woman wants a thing badly enough, she will actually believe it to be a necessity, even if it is only a wholly useless bit of ornament or a piece of equipment inferior to and less fitted to its purpose than one which she already has. Very often this type of wife cares little about her husband's activities except insofar as they involve the expenditure of the money which she must have to satisfy her psychologic necessities. Since this is a form of dominance, the sequelae are similar, except that divorce, with adequate alimony, is often a solution.

The possessive or jealous wife lives in a nightmare of suspicion as to her husband's thoughts of other women and his relations with them. Almost invariably this type of woman suffers from an inferiority complex reaction. If her husband indicates the slightest evidence of approval of any other woman, the wife reacts by feeling that his approval indicates an invidious comparison. It is impossible for such a woman to conceive that her husband could feel admiration or friendship for a woman without a direct sexual element which sooner or later would be fulfilled. The husband of such a woman is apt to do one of three things: to escape suspicion by associating only with men, thereby eliminating his wife from his social and recreational activities and creating another form of resentment; to become a recluse; or to feel

that he may as well seek the pleasures of extramarital female companionship, since he is already having to pay for them. There is a marked difference between male and female jealousy. The average man is not apt to feel a sense of serious jealousy unless there is definite evidence that his wife is being importuned by, or has yielded to, another man. His resentment is chiefly toward the man who has dared soil the object of his sacred devotion and not toward his wife, even though she were the instigator of the whole affair. The husband's resentment toward his wife is engendered only when he becomes convinced that she has willingly conspired toward her own soiling. The average woman, on the other hand, is, because of her innate egocentrism, constantly loaded with jealousy which awaits only the most trivial or even imagined event to flame into explosion. Her resentment is equally toward her husband and the "other woman" because she herself has been wounded.

The flirtatious wife: Practically every married woman feels that it is her inalienable right to associate with men (even tête à tête), to invite them as guests, to accept their escort within the limits of local convention, to accept or give a lift in an automobile, to speak of them as friends, to discuss their virtues and attractiveness, and otherwise to act as if she and they were reasonable human beings. All of these privileges are denied to most husbands. Many women extend their association with men to physical contact—holding hands, close dancing, and snuggling—and to provocative facial expressions and conversation. Such women usually explain their flirting on the basis that they derive pleasure from observing the reactions of their victims: as many express it, "It's fun to make them squirm." This, of course, is in the nature of revenge on the part of women who feel a subconscious inferiority to men.¹ Other women admit that they derive a sense of satisfaction of their sex ego through the flattery implied in the reaction induced in the man. When the process goes beyond this point to any degree up to, and including, actual seduction, relatively few women are impelled by actual desire for coitus. The majority of such women are frigid: some are seeking a substitutional stimulus which will enable them to escape from their impotence or relative frigidity toward the husband; some are seeking the satisfaction of a sense of revenge upon an actually or supposedly indifferent or unfaithful husband; others are only exhibiting their reaction to an inferiority complex due to total frigidity.

The martyred wife satisfies her inferiority complex through self-pity and the effort to induce pity in others. Even the most trivial disappointments and quarrels are magnified into major acts of brutality on the part of the husband, and the disease is of course constantly progressive. Practically all such women develop protean psychoneuroses, and many superadd jealousy and suspicion. Conversely, the primarily psychoneurotic wife is apt to superadd martyrdom.

The hypochondriac wife is usually the victim of the mode of physical and mental life which women have so assiduously cultivated during the recent progress of civilization. During adolescence and early maturity, most girls will adopt one of two attitudes. One group, chiefly composed of those who have been reared in the atmosphere of the worship of their beauty, will avoid any form of sport or real exercise in order to avoid marring in any way so wonderful a work of Nature. These girls, as women, are physically flabby and functionally below par. The other group, either to compensate for lack of beauty or because of some survival of a natural instinct, will keep up with the boys in sports and outdoor recreation. When these girls settle down to the physical inactivity of domestic life, the reaction makes the inevitable functional disturbances more acutely felt. The same applies to mental life. The girl accustomed to the intense mental activity of college work suffers greatly from the letdown to the mental stagnation of housekeeping, with its ample opportunity for introspection: To this extent, higher education which will not be continued or made use of after marriage is definitely deleterious to women. Hypochondriasis is very often the result of the woman's attitude toward, and technique of, housekeeping and other duties and to her almost total lack of recreational resources. Women have very few recreational resources, almost none which involve enough exercise to maintain physical fitness. Almost every man has one or more diversions, usually involving physical exertion, about which he daydreams and to which he looks forward with pleasure. Women can rarely think of anything to do in their spare time. Men enjoy muscular exertion for its own sake. Women generally dislike it intensely. Most men feel the necessity for physical recreation and find their greatest pleasure in natural and more or less primitive avocations; most women, especially as they grow older, find pleasure only in wholly artificial occupations, such as "social" activities, the religion of clothes, etc. The necessity for killing a great deal of time plus the lack of intellectual resources and an innate interest in people rather than in things is the reason for the love of gossip as a feminine trait.

Parenthetically, it may be said, the ideal wife recognizes that her husband has rights in all things equal to her own, with final authority over the expenditure of the money which he earns; she devotes her affection and her interest primarily to her husband, not to her appearance, her social activities, her house, or her children; she recognizes his right to choose his own friends and makes of them her own friends as well; she allows her husband one day and one evening a week for his own unquestioned recreation; she permits him to set his own limit on the fatigue and loss of sleep involved in social activities; she recognizes that one of her supreme functions is to alleviate the worries of his business life through cheerful sympathy, not to increase them by translating them into the terms of their reaction upon herself; she accepts her duties and responsibilities as equably as does her husband;

she is frank, straightforward, prompt, and fair in the settlement of differences; she does not resort to tears, sulking, nagging, or other subterfuges to win a battle lost on the basis of right, logic, and common sense; she keeps herself physically and mentally fit through occupations and recreations of both types; she is neither flirtatious, jealous, nor suspicious; and she remains throughout her life the eager and spontaneous lover and recipient of his love.

Women in Relation to Other Women

Biologically, every female animal is in competition with every other female, and jealousy is a characteristic instinct. In woman, this basic state is magnified through intelligence, the practice of monogamy, the economic aspects of civilized marriage, and the systems of caste and social competition to a point where every woman regards every other woman as at least her potential enemy. This enmity is so marked that women almost habitually derive a sense of satisfaction from making another woman uncomfortable—even going out of the way to do so. Cutting remarks to and about each other, the widespread tendency to preach disaster to prospective mothers and candidates for operation, and the well-recognized general “cattiness” are all evidences of this mental trend. Rather curiously to the male mind, the greater this feeling between two or more given individuals, the more it is apt to be masked by excessive demonstrations of superficial affection. Two women in competition for the attentions of the same man are almost certain to be in constant association with each other and mutually demonstrative both verbally and physically of a wholly false affection for each other. This can be explained on the basis that each woman is striving to discover and to imitate the traits and mannerisms in the other which are or may be pleasing to the man in question. Women very generally have a complete distrust of the sexual morality of other women. Wives in particular feel that, given opportunity, almost any other woman will attempt the seduction of their husbands and that their husbands will prove to be easy victims. Rather curiously, a woman is apt to regard her own chosen friends or the members of her social circle as being more or less above suspicion in this regard, yet the histories of many cases of infidelity indicate that seduction is more often attempted or accomplished by the wife’s chosen friends than by the husband’s casual or business associates.

Women in Relation to Employment

The attitude of women toward employment varies with their original environment. The girl who knows that she must support herself is a good and willing worker, whereas the girl from a well-to-do family is almost always averse to any work which does not carry with it some degree of glamour—egocentrism is apt to make her feel that she is conferring a favor by working and that she has a right to prescribe

the hours and conditions of her job. The chief ambition of women generally is to acquire a husband who will relieve them of the necessity of doing any work not of their own choosing, and they are very generally apt, if circumstances permit, to do no work of any sort. The fulfillment of this ambition, however, is disastrous: the leisure time provided by idleness furnishes ample opportunity for introspection—and introspection leads to a host of psychoneuroses. It is obvious that sex, as a submerged factor, influences the relations between men and women employed on a common task. Women will do their work better, more cheerfully, and more loyally for a male than for a female employer or director. Moreover, they acquire more or less of the masculine sense of the value of teamwork, and to an equivalent extent improve and strengthen their qualifications for successful wifehood. The working woman must of necessity abandon that peculiarly female and well-loved type of logic, almost paranoid in its perversion of premises and conclusions, which is so irritating to men and so productive of mental harm to women. It is also obvious that business relations afford an opportunity for women to fulfill whatever motivation they may have in the direction of marriage, yet a surprisingly small percentage of working women do so. The majority of these are activated by the "meal-ticket" motive, and failure (if not too often repeated) creates very little psychologic trauma. On the other hand, the employee who is unfortunate enough to fall truly in love with her employer is certain to develop severe mental reactions. She may, with the amorality of the woman in love, offer herself to him, or as is more often the case, subjugate her natural instincts to a life of selfless and sexless devotion to his interests. In spite of the humorous magazines and the self-styled sophisticates, the gold-digging immoral siren is a comparatively rare species in most American communities.

The attitude of woman toward work itself is complex, particularly at this time, when many women are undergoing cataclysmic changes in their modes of life, are being dislocated from their normal environments, and are being subjected to intense emotional stresses. At the same time, they are trying consciously or unconsciously to adapt themselves to the conflicts and frustrations incident to the revolutionary shift from a biologically natural life of reproduction and maternity to the biologically inconsistent pseudo-male life which their leaders have thrust upon them and which they so eagerly accept. In normal times, the majority of employed women work only as a matter of self-maintenance until they can reach the haven of support by a husband. The aspects of employment as a conditioning process for successful marriage have already been touched upon. There is also a type of woman, usually totally frigid and sexless or psychologically masculine, who regards work either as does the average man or (unconsciously) as a substitute for a nonexistent sexual life. A far greater number of superficially similar women are fundamentally normal yet consciously

suppress their normal motives and reactions. Most of the so-called career women fall in this group. In such cases, there is usually an element of psychologic trauma which has created an inferiority complex with regard to their actual sex. Women of this type usually develop one of two sequelae: They may fall in love, with a resultant cataclysmic conflict, or, far more often, they realize their error too late, with a resultant frustration complex. Psychoneuroses of extreme degree are likely to develop in these women. It is most rare that their behavior problems and psychoneuroses are escapable or remediable.

Another peculiarity of women is that, given say six duties which must be performed in the course of a day, they cannot isolate these duties. While they are actually performing task 1, they are simultaneously mentally planning for all of the other five; and when task 6 is reached, they are still mentally rehearsing the previous five. This plus the fact that women habitually expend a ton of nervous energy on an ounce of physical performance, leads to the daily occurrence of profound nervous fatigue or even exhaustion. These two tendencies, in regard to the performance of work, make of housekeeping a profoundly exhausting task. In addition, the utter monotony of this normal occupation generates of itself a host of psychoneuroses, and the great amount of spare time affords ample opportunity for magnification of these psychoneuroses through introspection.

When a woman, through persuasion or through previous business training, systematizes her housework, a great void of unoccupied time is created. The artificially inculcated lack of resources for physical and mental diversion make of this spare time a mere breeding ground for further introspection and increased psychoneurosis.

These are some of the aspects of the mental life of woman which underlie the development of various psychoneuroses. It is with the greatest trepidation that I, an untrained and almost unread amateur in both psychology and psychiatry, should venture to present before you an address of this type. It is only through my conviction that the psyche plays as large a part in the practice of gynecies as do the reproductive organs themselves that I could persuade myself. It is my hope that this may serve as a stimulus to more informed studies of the female mind to the ultimate welfare of the gynecic patients of the future.

THE SPASMOLYSANT ACTION OF MAGNESIUM IONS ON THE TETANICALLY CONTRACTING HUMAN GRAVID UTERUS*

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ONE of the truly urgent desiderata in the field of obstetrics and gynecology has been the evolution of a therapeutic agent which would effectively and efficiently exert a spasmolysant effect upon the myometrium. Abnormalities of uterine contractions characterized by spasm are evident in the so-called spasmodic type of dysmenorrhea, and in the afterpains experienced by many multiparous women. In addition, tetanic uterine contractions are not infrequently observed when labor is induced by means of oxytocics especially posterior pituitary extracts.

In this report it is proposed to offer substantial graphic evidence of the fact that the magnesium ion may exert a very effective spasmolytic effect upon the tetanically contracted human gravid uterus. As a matter of fact, magnesium offers promise of being an ideal myometrial "sedative" in many ways.

It seems pertinent at this point to review briefly certain pharmacologic activities of magnesium with especial reference to muscle physiology, particularly that of the uterus.

Vulpian, in 1869, was the first to demonstrate the "paralyzing" action of magnesium on muscle. This finding was extended by his students, Jolyet and Cahours (1869), to show that magnesium exerted a curare-like action on the neuromuscular synapse. Further investigations since then have revealed that magnesium raises muscle chronaxie but not that of the nerve supplying the muscle (Wodon, 1931; Hazard and Wurmser, 1931; Bresnan and Boyd, 1937). Meltzer and Aver (1905-1912), in a classic series of experiments on the pharmacodynamic activities of magnesium, discovered its central depressant action as well as its ability to relax certain sphincters whose motor impulses are supplied by the sympathetic chain, such as the sphincter of Oddi. Trendelenburg (1912) reported the relaxing effect of magnesium on the smooth muscle of the bronchial tree, while Rozen and Perusse (1929) noted a similar effect upon the gastric musculature. Hazard and Wurmser (1932) demonstrated that arteriolar muscle was relaxed by the magnesium ion. For more comprehensive reviews, the reader is referred to those of Rico (1935), Greenberg (1939), and Sollman (1942).

The effects of magnesium, however, upon the uterus are of particular concern here. Van Dyke and Hastings (1928), in studying the response of the isolated guinea pig uterus in different ionic en-

*Foundation Prize Thesis presented at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1914.

vironments to posterior pituitary extracts, found that (1) the absence of Mg^{++} ions resulted in a decreased response; (2) a concentration of 1 millimol produced an optimal response; (3) a concentration of 3 millimols caused a depression in the response of the isolated uterus. Further investigation of the problem of magnesium ion concentration and the response of isolated uterus were carried out independently and almost simultaneously by Genell (1938) and Fraser (1939). These studies, which confirmed each other, revealed that the addition of magnesium ions to a magnesium-free bath increased the oxytocic response of the isolated uterus to whole posterior pituitary extracts (pituitrin), to the oxytocic fraction (pitocin), and to the vasopressor factor (pitressin). When the concentration of magnesium was from 100 to 200 mg., this increase of oxytocic potency ranged from five to ten times that in a magnesium-free bath. Interesting, indeed, was the finding that 1 pressor unit of pitressin, which had 0.05 oxytocic unit in a magnesium-free bath, was exactly equal to 1 oxytocic unit—an increased oxytocic potency of 2,000 per cent—when the concentration of magnesium was 100 mg. When the concentration of magnesium ranged from 200 to 300 mg., the oxytocic effect of the various posterior pituitary extracts was diminished, and at a concentration of from 500 to 1,000 mg., the uterine response was inhibited.

Wodon (1929) was first to demonstrate the spasmolytic action of magnesium. Using the isolated guinea pig uterus rendered tetanic by posterior pituitary extract, he observed that adding successive 20 mg. doses of magnesium chloride to the bath resulted in a progressive detetanicization of the uterine muscle. At a concentration of 200 mg., rhythmic intermittent uterine contractions reappeared. As the concentration of magnesium was further increased, uterine contractions gradually diminished, finally disappearing at a concentration of 1,000 mg. of magnesium. LaBarre and Wodon (1929) observed relaxation by magnesium *in vivo* of a decerebrated cat's uterus which had been rendered tetanic by pitocin.

Further observation by Wodon (1929) (1931) disclosed that Mg^{++} ions could abolish myometrial tetany induced by a variety of agents including ergotoxine, acetylcholine, pilocarpine, quinine, histamine, and barium. Reynolds (1935) using the unanesthetized rabbit uterus noted that magnesium would bring about relaxation with resumption of spontaneous intermittent contractions when the uterus was undergoing sustained contractions in response to calcium salts.

As far as the human uterus is concerned, Wodon (1931), in discussing the use of magnesium salts in eclampsia, makes mention of the fact that he successfully utilized the antispasmodic properties of magnesium sulfate in abolishing uterine tetany as sometimes occurs in eclampsia and in one case of uterine tetany resulting from quinine. At no time, however, did Wodon present any graphic evidence to this effect.

In review, then, it seems clear that the magnesium ion may, in adequate concentration, exert a relaxing effect upon the uterus. The action appears to be a direct one upon the myometrium since it takes place both *in vivo* and *in vitro*. Significantly, magnesium in small concentrations not only does *not* abolish rhythmic intermittent uterine contractions but actually seems to enhance them (Wodon, 1931; Genell, 1938; Fraser, 1939). Some years ago, Prof. Samuel R. M. Reynolds, while discussing the effects of various ions upon the uterus with me, sug-

gested that, theoretically at least, the magnesium ion should prove to be an ideal uterine "sedative." Further, he suggested its clinical trial in cases of spasm of the uterus.

Procedure

Our interest in the problem of the effects of magnesium on the human uterus arose while we were investigating the problem of the onset and course of labor particularly from the viewpoint of patterns of motility. One of the lines of attack was to study normal patients in labor and then compare these norms with the motility response of the human gravid uterus to various oxytocic drugs. External hysterography by means of the Lorand tocograph as modified by Murphy was used. The apparatus has been fully described by Murphy (1940). Briefly, its operation is based on the fact that when the apparatus is placed upon the abdomen, a small button 1 cm. wide and 1 cm. long impinges upon the anterior abdominal wall against the anterior uterine wall. When the uterus contracts, it bulges anteriorly, pressing upon the small button. Since this button is connected by a series of levers to a writing arm, the contraction is recorded as a rise from the base line in the form of a curve. The apparatus is not sensitive enough to record respiration but will record hearty laughing or coughing and sneezing (as straight up and down lines). Fetal movements are also recorded as straight lines if they occur directly against the small buttons.

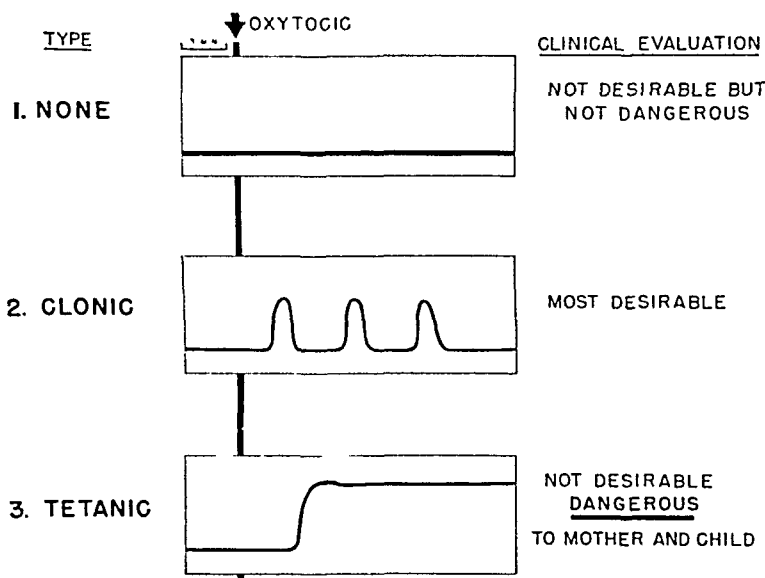


Fig. 1.—Patterns of uterine motility. Principal types of pharmacodynamic response of the human gravid uterus to oxytocics.

The apparatus is left upon the abdomen for a control reading of fifteen or twenty minutes. At the end of that time, the drug to be studied is administered and the effects studied for a test period of from thirty to sixty minutes. To date over eleven hundred (1,100) tracings have been made. The oxytocic effects of pituitrin, pitocin, pitressin, quinine, adrenalin, neostigmine, ergonovine, and a synthetic

ergonovine-like drug (d-l-lysergic acid—hydroxybutylamide)* have been studied as well as the effects of calcium and magnesium ions upon the responses so induced.

In Fig. 1 are illustrated the basic types of response of the gravid uterus to oxytocics. There may be no response, or just a simple rise in tonus. The contractile response may be clonic, with or without a rise in tonus, or it may be tetanic. The latter may be incomplete, that is, small intermittent contractions may be apparent, while a spontaneous resolution soon takes place in from three to five minutes followed by clonic contractions. On the other hand, the tetany may be of the complete variety. Tetany was judged to be complete if the patient complained of more or less severe pain, while the contraction phase had to be sustained for a minimum of six minutes, and the uterus was palpable as a firm hard ligneous mass into which the fingers could not be impressed.

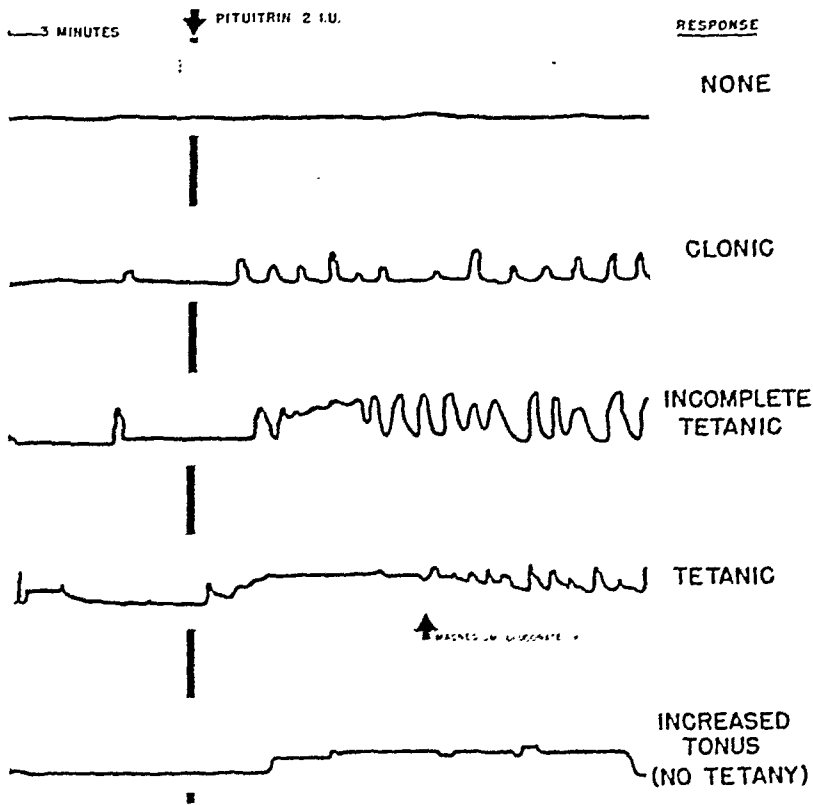


Fig. 2.—Patterns of uterine motility induced by posterior pituitary extract (pituiratin).

Early in our studies we were impressed with the fact that the human gravid uterus varies greatly in its sensitivity to oxytocics. As a marked general rule, however, the response of the same individual to the same dose of the same drug tended to be similar. For example, if a tetanic response is observed on one occasion, the following week the same response will occur. In Fig. 2 four typical responses to whole posterior pituitary extract (pituiratin) are illustrated. Essentially similar responses occur to pitocin, pitressin, quinine, ergonovine and methergine.

*Produced commercially as Methergine by Sandoz Chemical Works, Inc., New York, N. Y.

Effects of Magnesium Ion Upon Uterine Tetany

Complete tetany is obviously the most undesirable of any of the responses of the uterus to oxytocics, the dangers being fetal asphyxia, permanent cerebral damage to baby if it lives, or uterine rupture. During repetition of Murphy's work (1940, 1941) tetany of the uterus of varying duration and severity was observed many times but as a rule tended to be mild and of short duration (incomplete variety). Very early in our studies, however, we encountered one individual who complained of severe abdominal pain, continuous in character, while the uterus remained hard as stone. When the spasm did not disappear, the suggestion of Prof. S. R. M. Reynolds was recalled to mind. Accordingly, 10 c.c. of a 20 per cent $MgSO_4$ solution were given intravenously. Before the needle was withdrawn from the vein, the tetany of the uterus had been completely abolished. Moreover, the uterus continued to contract intermittently and rhythmically. The pain was completely relieved within sixty seconds. (Fig. 3, A.)

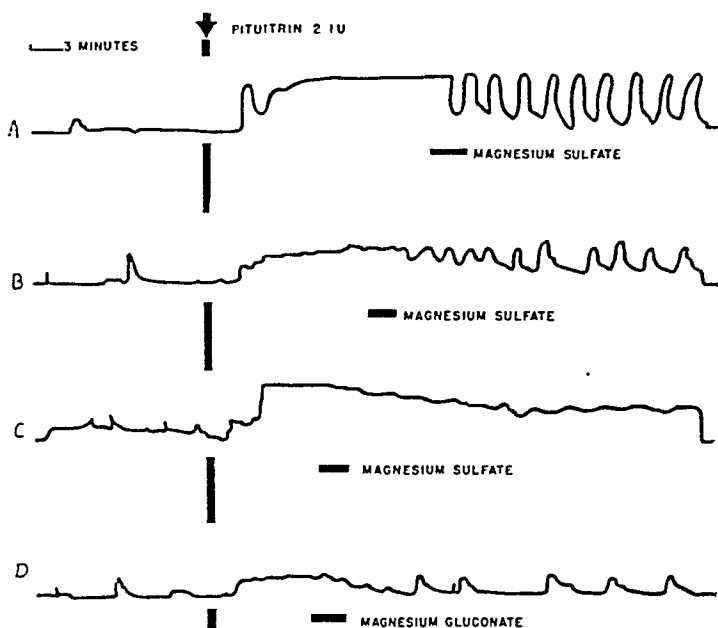


Fig. 3.—Patterns of uterine motility. Types of spasmolysant effect of magnesium ion (magnesium sulfate; magnesium gluconate) upon induced uterine tetany.

To date, over sixty instances of painful tetanic contractions of the human gravid uterus have been induced by means of the following drugs: (1) whole posterior pituitary extract (pituitrin), 0.5 to 2 international units (I.U.); (2) oxytocic fraction of posterior pituitary (pitocin), 0.5 to 2 I.U.; (3) vasopressor fraction of the posterior pituitary, 0.5 to 2 pressor units (approximately 0.025 to 0.10 oxytocic I.U.); (4) ergonovine tartrate, 12.5 to 50 gamma; (5) methergine (synthetic product closely related chemically and pharmacologically to ergonovine), 12.5 to 50 gamma; (6) quinine—(a) oral, 5 to 10 gr. (0.3 to 0.6

Gm.); (b) intravenously as calcium-quinine,* 5 to 10 c.c. quinine gluconate (0.06 Gm. per cubic centimeter).

Regardless of the oxytocic agent that produced the painful tetanic contraction of the gravid human uterus, the magnesium ion completely relieved the pain within thirty to ninety seconds and at the same time brought about relaxation of the myometrium. The latter effect is illustrated in Fig. 3.

In order to prove that the magnesium ion was the one responsible for the relaxing effect upon the myometrium, two ionized salts of magnesium were used—the sulfate and the gluconate. Magnesium sulfate was given intravenously as 2 c.c. of the 50 per cent solution, or 10 c.c. of the 20 to 25 per cent solution. Magnesium gluconate was administered intravenously as 10 c.c. of the 20 per cent solution. Since both salts brought about detetanization of the uterine musculature, it can be regarded as proof that the magnesium ion was the one responsible for the relaxation effect. No attempt was made to quantitate the spasmolysant action of magnesium at various dose levels. The only bad side effects noted were nausea and/or vomiting if the solution was given too quickly. At least from three to five minutes should be taken in administration of these solutions.

The spasmolysant effect of the magnesium ion upon uterine tetany varies in different individuals. This is well illustrated in Fig. 3. In the first one (3, A) the usual response observed is graphically presented. Not only is the spasm abolished, but regular rhythmic intermittent contractions appear. Note that the height of each contraction is the same as that at the time of tetany.

In 3, B the response may be divided into two phases: First, intermittent rhythmic contractions appear quickly; second, myometrial tonus returns to or toward the base line gradually, even though the patient no longer feels any pain while the palpating finger can be easily impressed into the uterine wall and the fetal heart rate becomes normal once more. This type of response is the second most common.

In Fig. 3, C the effect of magnesium ion upon the tetanically contracted human gravid uterus is characterized by a slow gradual return of myometrial tonus to the base line of the pre-experimental level, while intermittent rhythmic contractions are also slow in appearing. The pain was completely relieved.

In Fig. 3, D, the same response to magnesium gluconate as to magnesium sulfate is clearly illustrated.

Prevention of Induced Uterine Tetany

Since it had been determined that magnesium could effectively abolish tetany, it was next decided to determine whether magnesium would be able to prevent tetany. Accordingly, twelve were chosen who had

*Calgluquine of Sandoz Chemical Works, Inc., New York, N. Y.

previously shown tetany on one or more occasions to 2 I.U. (3 minims) of whole posterior pituitary hormone (pituitrin). Two series were run. In the first, each patient was given either 2 c.c. of 50 per cent magnesium sulfate or 10 c.c. of 20 per cent magnesium gluconate three to five minutes *before* she received 2 I.U. of posterior pituitary hormone.

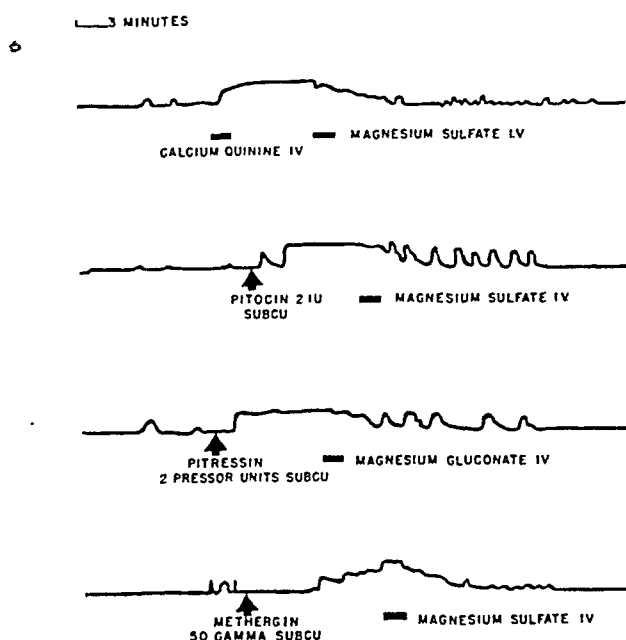
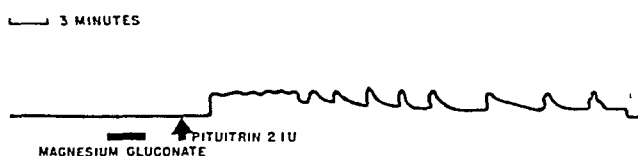
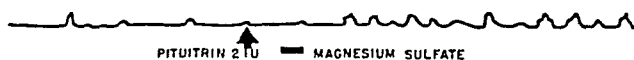


Fig. 4.—Patterns of uterine motility. Spasmolytic effect of magnesium ion on uterine tetany induced by various oxytocics.

MAGNESIUM FOLLOWED BY POSTERIOR PITUITARY EXTRACT



POSTERIOR PITUITARY EXTRACT FOLLOWED BY MAGNESIUM



PROPHYLACTIC ANTI-SPASMODIC EFFECT OF MAGNESIUM ION

Fig. 5.—Patterns of uterine motility. Prevention of induced uterine tetany by magnesium ion. Importance of sequence of administration of oxytocic and magnesium.

In seven of these patients some form of tetanic response occurred. On the other hand, when the same patients received the same dose of magnesium salt three to five minutes *after* the same dose of oxytocic, only a mild incomplete tetanic response was observed in but two patients.

It seems clear, then, that the magnesium ion is able to prevent induced tetanic contractions of the human gravid uterus. It is best administered, however, some three to five minutes after the oxytocic is given (Fig. 5).

Effect of Calcium Ion Upon Uterine Tetany

In ten patients with induced uterine tetany, 10 c.c. of 10 per cent or 20 per cent calcium gluconate were administered intravenously. The effects observed were quite variable (Fig. 6). In three patients, the tetany was seemingly rendered even more painful and intense, necessitating immediate administration of magnesium for relief. In five, no effect at all was observed until magnesium was given. In the remaining two patients there seemed to occur some relief from the pain while the uterus did seem to become softer. In review, it is felt that the results noted in the last two patients were probably coincidental. Certainly, it is obvious that the effects of calcium ion are variable and unpredictable while the magnesium ion always produces relaxation.

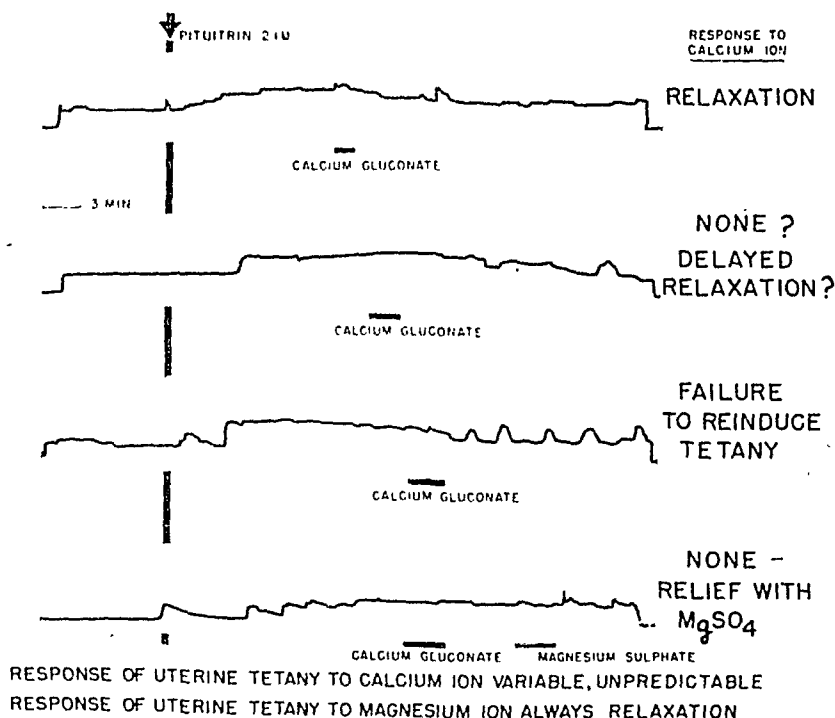


Fig. 6.—Patterns of uterine motility. Variable effects of calcium ion on tetany of human gravid uterus induced by posterior pituitary extract (pituitrin).

Effect of Magnesium Ion on Normal Labor

After the first stage of labor had become definitely established in a group of primipara, magnesium ion was administered. No observable effect was noted upon the pattern of uterine motility. Several patients noted that the amount of pain with each contraction was reduced. In some, the relief was so marked that repetition of the same dose of magnesium ion at two- to three-hour intervals was all the analgesia

needed. In others, the synergistic action of the magnesium ion with morphine or barbiturates was clearly manifest, necessitating much smaller doses of these drugs.

Clinical Applications

1. *Induction of Labor With Oxytocics.*—This procedure may often result in tetany of the human gravid uterus. Though it is most commonly observed after the use of posterior pituitary hormone, we have also noted tetany after 0.3 Gm. (5 gr.) of quinine. The dangers of tetany are rupture of the uterus, death of the fetus by asphyxiation, or, if the baby lives, possible permanent damage to its brain. Once tetany is present, it can immediately be relieved by intravenous magnesium salts. Better still, tetany can be usually prevented by administering the magnesium ion, preferably magnesium gluconate for its seemingly longer action (10 c.c. of 20 per cent solution), some three to five minutes after the oxytocic is given. Tetany can come on, however, anywhere from two to twenty minutes after the oxytocic is given. In view of our experience, it is strongly felt that one should never administer more than 1 I.U. of posterior pituitary hormone at a time. This corresponds to $\frac{1}{10}$ c.c. (0.1 c.c.) or 1.5 minims. *Moreover, this volume can be accurately measured only with a tuberculin syringe.* Furthermore, because of the added magnesium, the oxytocic response is considerably enhanced (Genell, Fraser).

These findings were recently confirmed in a most dramatic manner. A multipara developed secondary inertia when practically fully dilated with the head in the left iliac fossa. One minim of pituitrin (0.66 I.U.) was given subcutaneously. The uterus responded in a sustained tetanic contraction. (In such cases, both upper and lower portions of the uterus contract almost simultaneously, grasping the baby in a viselike hold, thus preventing expulsion of the fetus.) The fetal heart rate dropped from 128 to 4 per minute. Within sixty seconds after the administration of 10 c.c. of 20 per cent magnesium sulfate intravenously, the hard, ligneous uterus became soft. The fetal heart soon was back to normal. Version and extraction resulted in a living baby. There was a moderate amount of postpartum bleeding which came in spurts as the uterus contracted intermittently. Unfortunately, calcium salts were not available, but with massage and large doses of ergonovine, the bleeding was controlled.

2. *Incarcerated But Separated Placenta in the Third Stage.*—Since the administration of oxytocics during the second stage of labor (after the anterior shoulder is born) is becoming more widely used, cases of separated placenta incarcerated in the uterine cavity by the induced tetany have become much more frequent. To date, we have seen six cases, five after ergonovine and one after pitocin. In each instance, following the administration of 2 c.c. of 50 per cent solution of magnesium sulfate intravenously, the uterine tetany was abolished and the placenta was easily expelled by the modified Credé method. In one instance, some bleeding occurred as the uterus began to contract intermittently. Intravenous calcium gluconate (10 c.c. of 20 per cent solution) soon brought about a firmly contracted uterus.

3. *Bandl's Ring*.—Although I have had no personal experience with the use of the magnesium ion in this condition, I was recently told of a case in which a Bandl's ring was encountered in a toxemic patient. Soon after the administration of intravenous magnesium sulfate, given for the toxemia, the Bandl's ring melted away.

4. *Afterpains*.—Though afterpains usually are present in multipara, they rarely present a marked clinical problem except when ergonovine is routinely used in the early postpartum period. Statistically, there is no doubt that routine use of oral ergonovine in the postpartum period definitely accentuates these pains. Magnesium gluconate, 1 Gm. orally three or four times daily, usually achieves marked relief or amelioration in a short time. The sulfate may also be used.

5. *Dysmenorrhea*.—The so-called spasmodic form of primary dysmenorrhea has been found to be easily relieved by the administration of magnesium salts at the actual time of pain. Ten cubic centimeters of 20 per cent magnesium gluconate will bring about complete to more than satisfactory relief for a period of from two to eight hours. As a prophylactic agent, 1 Gm. of magnesium gluconate four times daily or 1 dram of magnesium sulfate per os daily starting two weeks before the period is due often achieves very satisfactory relief both from premenstrual tension as well as the painful menses. (These results will be published separately.)

6. *Abruptio Placentae*.—After this report was submitted for publication, a case of abruptio placentae associated with a hard ligneous tetanically contracted uterus was seen. After 10 c.c. of 20 per cent magnesium sulfate, the uterus relaxed enough for short intermittent contractions to be palpable. After a second dose of magnesium sulfate fifteen minutes later, the uterus relaxed very markedly permitting intermittent rhythmic uterine contractions to be easily palpable and, in addition, the fingers could be easily impressed into the uterus. The amount of bleeding was not appreciably affected. The cervix seemed to soften and to dilate quite rapidly after the magnesium, but this may have been coincidental.

The clinical significance of this is twofold. First, of course, is the relaxation of the uterus. Second, is the fact that in muscle rendered tetanic and thus anoxic, certain toxins are released, which Young feels may be the cause of the toxemia so often associated with abruptio placentae.

Summary and Conclusions

1. The magnesium ion has been graphically demonstrated to exert an immediate spasmolytic effect upon the tetanically contracting human gravid uterus. Magnesium abolished tetany induced by the following oxytocic agents: posterior pituitary hormone—whole extract (pituitrin), purified oxytocic fraction (pitocin) and purified vasopressor fraction (pitressin); quinine, ergonovine, and methergine (a synthetic ergonovine-like substance). Satisfactory results were obtained by the intravenous administration of either 2 c.c. of 50 per cent solution of magnesium sulfate or 10 c.c. of 20 per cent solution of magnesium gluconate. Magnesium probably acts directly on the myometrium, slowing the rate of the contraction wave.

2. Induced uterine tetany may be prevented by the prophylactic administration of intravenous magnesium salts from three to five minutes after administration of the oxytocic agent.

3. Posterior pituitary hormone should not be given in a dose exceeding 1 I.U., that is, 0.1 c.c. (1.5 minims), and should be measured out in a tuberculin syringe.

4. Magnesium ion has no demonstrable effect upon the pattern of uterine motility in the first stage of labor. It does, however, exert a definite analgesic effect as far as the patient is concerned.

5. Calcium ion has little or no value as a spasmolysant upon induced uterine tetany.

6. Clinical applications for the use of the antispasmodic properties of the magnesium ion have been found in the following conditions:

A. Immediate relaxation of oxytocic-induced uterine tetany

1. During induction of labor or management of secondary degree uterine inertia.

2. Third stage of labor for a separated but incarcerated placenta.

B. Prevention of uterine tetany following use of oxytocics.

C. Relief of afterpains.

D. Alleviation of essential spasmodic dysmenorrhea.

E. Relaxation of Bandl's ring.

F. Relaxation of tetanically contracted uterus in abruptio placentae.

The author is particularly indebted to Dr. Samuel R. M. Reynolds and Dr. Howard F. Kane for their constructive criticisms, guidance, and help in evaluation of these studies during their progress. Dr. Douglas P. Murphy of the Gynecean Hospital Institute of the University of Pennsylvania, School of Medicine, was most kind in teaching the author how to use the Lorand tocograph properly. Through the courtesy of Dr. Caroline Jackson, patients at the Florence Crittendon Home, and, through Dr. John L. Parks, cases at the Gallinger Municipal Hospital were made available for clinical study.

The Sandoz Chemical Works, Inc., defrayed the major part of the expenses of these studies and, in addition, supplied the following material: Neo-calglucon (calcium gluconogalactogluconate) in 10 per cent and 20 per cent concentration; calcium quinine solution (Calgluquine); magnesium gluconate in 20 per cent solution; ergonovine tartrate (Basergin); and (d-l-lysergic acid-hydroxybutylamide) methergine.

Parke, Davis and Company generously supplied posterior pituitary hormone as whole extract (Pituitrin), oxytocic fraction (Pitocin), and vasopressor fraction (Pitressin).

References

- Fraser, A. M.: *J. Pharmacol. & Exper. Therap.* 66: 85, 1939.
 Genell, S.: *Skandinav. Arch. f. Physiol.* 80: 124, 1938.
 Greenberg, D. M.: *J. Biol. Chem.* 114: 43, 1936.
 Hazard, R., and Wurmser, L.: *Compt. rend. Soc. de biol.* 107: 453, 1931; 110: 525, 1932.
 Jolyet, F., and Cahours: *Arch. de Physiol.* 2: 113, 1869.
 LaBarre, J., and Wodon, J. L.: *Compt. rend. Soc. de biol.* 103: 530, 1929.
 Meltzer, S. J., and Auer, J.: *Am. J. Physiol.* 16: 233, 1906.
 Murphy, D. P.: *AM. J. OBST. & GYN.* 39: 808, 1940; 41: 274, 1941.
 Reynolds, S. R. M.: *Am. J. Physiol.* 105: 358, 1933.
 Rico, T.: *Arq. de Path. (Lisbon)* 5: 205, 1933.
 Rozen, J. S., and Perusse, G. L.: *Am. J. Physiol.* 91: 298, 1929.
 Sollman, T.: *A Manual of Pharmacology*, ed. 6, Philadelphia, 1942, W. B. Saunders Co.
 Trendelenburg, P.: *Arch. f. exper. Path. u. Pharmacol.* 69: 79, 1912.
 Van Dyke, H. B., and Hastings, A. B.: *Am. J. Physiol.* 83: 563, 1928.
 Vulpian: Quoted by Jolyet and Cahours.
 Wodon, J. L.: *Compt. rend. Soc. de biol.* 103: 529, 930, 1929
 Wodon, J. L.: *Arch. Internat. de méd. expér.* 6: 245, 1931.

HYSTERECTOMY WITH PRESERVATION OF OVARIAN TISSUE IN THE TREATMENT OF ENDOMETRIOSIS*

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IT IS generally accepted that removal of both ovaries or castration by radiation therapy will relieve the symptoms and cause the lesions to subside in endometriosis. As this condition is encountered frequently in patients in the third and fourth decades, one hesitates to employ such a radical procedure and precipitate the menopause in women so young unless there is no other satisfactory method of giving relief. In the younger patients, particularly, it is our belief that nonoperative treatment should be practiced as long as it seems feasible, judging from the severity of the symptoms and the extent of local involvement. Therefore, these patients are kept under observation, at times for years. When operative treatment is finally decided upon, the aim should be to get them well without multiple laparotomies. The policy of deferring laparotomy until the patient is older, if disability does not force the issue, results in fewer reoperations and better end results. When unsuspected endometriosis is encountered in the course of a laparotomy in young patients, preservation of uterus and ovarian tissue should be carried out if there seems to be a possibility of pregnancy, and if the symptoms are not too incapacitating. The frequent association of endometriosis with fibroids or other pelvic pathology too often makes conservative operations futile as to childbearing and undesirable for the future welfare of the patient. Dysmenorrhea is one of the most common symptoms, and as sterility is common in endometriosis and almost the rule when the disease is extensive, the results of conservative operations are often disappointing.

Marked and prolonged vasomotor and nervous symptoms may occur when the menopause is produced suddenly in young patients, so we have been interested in the conservation of ovarian tissue in the treatment.

Operative Procedures

Formerly we removed both ovaries in extensive endometriosis regardless of the age of the patient. In less extensive cases, when one ovary was involved and the other one seemed negative, only the one ovary would be removed and attempts were made to excise or fulgurate the outlying implants. Some of these patients required second operations.

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CASE 1.—Mrs. E. S., aged 34 years, St. Francis Hospital, gynecologic No. 26-170. Pain in left lower quadrant, dysmenorrhea, and mass in region of left adnexa. On March 31, 1926, the left adnexa were removed for an adherent chocolate cyst of the left ovary about 6 cm. in diameter. An indurated mass 2 cm. in diameter was binding the rectum to the cervix. Pathologic report: *Endometrial chocolate cyst of ovary*. The dysmenorrhea and at times intermenstrual bleeding continued after operation. She had attacks of pain in the right lower quadrant at times and in a few years nodules could be felt in the cul-de-sac. In May, 1933 (seven years after the above operation), she returned, complaining of increasing constipation for four weeks and no bowel movement for the preceding five days in spite of enemas. Abdominal cramps had been present for twenty-four hours. There was moderate distention of the abdomen, and x-ray examination revealed a distended colon and ampulla of the rectum, with a segment above the ampulla that showed no gas. Barium enema would not pass this point. On May 24, 1933, laparotomy was performed and the uterus, rectosigmoid, and right adnexa were found bound together in a nodular mass with puckering and dark areas typical of endometriosis. The colon was distended above the mass. A first stage colostomy was done and two days later the bowel was opened. A week later artificial menopause was induced with radium. Two months later the patient was passing feces through the colostomy and through the anus. In March, 1934, a barium enema flowed freely out of the colostomy and no evidence of obstruction was seen on x-ray plate. Patient had learned to take care of her colostomy so well that she refused to have it closed. At present the patient feels well and no masses are felt on vaginal or rectal examination.

Remarks.—This patient, aged 34 years, was treated conservatively at operation and seven years later developed intestinal obstruction from endometrioma at the rectosigmoid junction, necessitating a colostomy.*

CASE 2.—Mrs. M. F., aged 26 years, St. Francis Hospital, gynecologic No. 33-407. Severe dysmenorrhea, worse on the left side. Adherent, tender cystic mass in region of left adnexa and nodules palpated in the cul-de-sac. Operation, Oct. 31, 1933: Removal of left adnexa for endometrial chocolate cyst. Endometrial implants in the cul-de-sac and on the posterior surface of the cervix were fulgurated. Two years later the patient still complained of severe dysmenorrhea. Five years after operation patient returned complaining of a tender, firm nodule in the incisional scar which was particularly tender at the time of her periods. She stated that this had been present for one year. The mass was removed under local anesthesia. It was 2 cm. in diameter and was an irregular nodular mass which, on section, presented two dark areas. Pathologic report: *Endometrial adenoma in scar*.

Remarks.—This patient was treated conservatively at operation at the age of 26 years. Five years later she still had severe dysmenorrhea, and an endometrial adenoma had developed in the scar.

In the treatment of endometriosis surgically our procedure now is to remove the uterus and major lesions in the ovaries, if present, and disregard the implants and to preserve all of the ovarian tissue possible. It is found that if the uterus is removed, no further trouble is experienced, and in none of the cases so treated has reoperation been done so

*Since this paper was written, the colostomy has been closed successfully.

far as can be determined in the follow-up study. Hysterectomy is not a conservative operation but it is much more conservative than radiation castration or bilateral oophorectomy. Ovaries are removed when they are much involved by chocolate cysts or too badly damaged as a result of separation of dense adhesions.

Rationale of Treatment

In certain cases when fibroids were accompanied by mild or moderate endometriosis and it was thought that the patient's symptoms were due chiefly to the fibroids, hysterectomy was done and one or both ovaries preserved intact. The patient's symptoms disappeared and there was no evidence of extension of the endometriosis later. This happened so frequently that an explanation was sought. It is frequently reported in the literature that ovarian function disappears within a few years after hysterectomy and this seemed to be the logical explanation of why the process subsided. Clinical observations have been against this viewpoint. We have patients who go through the typical menopause years after hysterectomy, indicating that the ovaries continue to function until the usual menopausal age. Periodic soreness of the breasts and periodic swelling and soreness of ovarian grafts for long periods after hysterectomy would indicate continuation of ovarian activity. Gross and microscopic examination of ovaries removed at a subsequent operation after hysterectomy have revealed active corpora lutea. Hormone assays in our endocrine clinic and laboratory (results to be published later) indicate that the ovaries continue to function for years after hysterectomy. Failure of ovarian function, therefore, does not seem to be the explanation for the clinical results from hysterectomy alone in endometriosis.

Theoretically it might be expected that there would be an increase in symptoms after hysterectomy with preservation of ovaries, as the full ovarian hormone action should then be exerted on the remaining endometrium in the islands or implants. Instead, a subsidence of symptoms and lesions occurs. I have seen marked dyspareunia, which resulted from tender nodules in the cul-de-sac, disappear within two months after hysterectomy alone and the nodules lose their tenderness almost entirely. Perhaps there is a pituitary-ovarian-endometrial relationship which is broken if the bulk of the endometrium is removed by hysterectomy. The explanation of the amelioration of symptoms and subsidence of activity in the nodules after hysterectomy raises a very interesting problem for solution and it is hoped that it will be possible to contribute the answer in our endocrine clinic and laboratory.

Another possible explanation is that removal of the uterus stops continued implantations of endometrium via the tubes (Sampson's^{1, 2} theory) and in that way causes the improvement. This is not likely, for, in 40 patients of the 155 in our follow-up series who had previous pelvic

operations, 11 had bilateral salpingectomy from one to ten years and one had bilateral tubal ligation fourteen years beforehand and the endometriosis continued.

Survey

In the Elizabeth Steel Magee and St. Francis Hospitals in Pittsburgh, 271 cases of endometriosis have been treated surgically on the services of the author and his associate, Dr. J. A. Hepp, in the last ten years. In the follow-up study, 155 cases or 57.2 per cent of the series were contacted. This series does not include the patients who were treated nonoperatively.

In the entire series the age groups are shown in Table I.

TABLE I. AGES OF PATIENTS AT TIME OF OPERATION

AGE GROUP (YEARS)	NUMBER IN EACH AGE GROUP	PER CENT IN EACH AGE GROUP
18-19	3	1.10
20-24	23	8.5
25-29	41	15.1
30-34	62	22.9
35-39	61	22.5
40-44	50	18.4
45-49	21	7.75
50-54	5	1.84
55-59	3	1.10
60	2	0.74
	271	

The largest number of cases (79 per cent) occurred between 25 and 45 years of age. Of 26 patients who were below 25 years of age, 10 had chocolate cysts of the ovary and 6 had endometriomas in old abdominal scars. The others had endometrial implants on the peritoneum or sacrouterine ligaments. There were 10 patients from 50 to 60 years of age, 3 of them were still menstruating and they had adenomyosis or adenomyomas of the uterus. The remaining 7 were past the menopause and the operations were done for other conditions (ovarian cysts, malignant and benign, prolapsus uteri, and one granulosa cell tumor of the ovary), and localized adenomyosis of the uterus was found.

One hundred and ninety-four were married and 137, or 70.6 per cent, gave a history of pregnancy. One hundred and twenty-eight, or 66 per cent, had children and the other 9 had had miscarriages. Seventy-seven or more than one-fourth of the total series were single.

Eighty-nine had fibromyomas and 19 had adenomyomas, or an incidence of 39.8 per cent myomas, which compares closely with Dannreuther's³ 40 per cent, Haydon's⁴ 44.4 per cent, and Fallas and Rosenblum's⁹ 41.5 per cent. Adenomyosis without fibroids was found in nine cases.

Chocolate Cysts

Chocolate cysts were present in 73 cases. It is sometimes difficult to differentiate grossly an endometrial chocolate cyst from a corpus luteum cyst with chocolate-like material, as is found at times when the ovary has been sealed in by adhesions as a result of a previous pelvic operation. In the 40 patients who had had previous pelvic operations, 5 had cysts with typical chocolate material but no endometrium could be found on microscopic examination so they are not included in this

series. Three patients had previous oophorectomy elsewhere for chocolate cysts and no hysterectomy was done. They returned with true endometrial chocolate cysts on the other side. One of these patients had had a spontaneous rupture of a chocolate cyst as reported by Novak¹¹ which was the reason for the first operation. The author has seen two cases of fatal postoperative peritonitis when chocolate cysts adherent to the colon were ruptured during the separation of adhesions and the abdomen was closed without drainage. Since then, drainage has been employed in that type of case. In one patient in whom drainage was employed, a nonhemolytic streptococcus was cultured from the chocolate material. The patient recovered. It is presumed that occasionally a chocolate cyst adherent to the colon may become infected directly from the colon.

Dyspareunia is a common symptom due to thickening and tenderness and adhesions of the peritoneum of the cul-de-sac and sacrouterine ligaments. Pain in the rectum, chiefly around the time of menstruation, may be a prominent symptom and it is not unusual to find the rectum indurated and adherent to the posterior wall of the cervix and uterus. There were two cases of distinct endometriomas of the wall of the large bowel at a distance from this usual site. There were two cases of endometriomas of the bladder wall involving the mucosa and showing blood in the urine periodically. I have had one case of endometriosis of the umbilicus, not included in this series. The management of these cases and those of endometrioma in the abdominal scar will be discussed in a subsequent paper.

There were two postoperative deaths, a mortality of 0.74 per cent in the 271 cases.

One hundred and sixty-seven or 61.6 per cent of the series had hysterectomy, of which 157 were subtotal and 10 were total. Five cases were treated with radium.

Follow-Up Series

In the 155 cases contacted in the follow-up series, the operations performed, the average age of the patient at operation, the average time of follow-up, and the results are given in Table II. Under *Improved* the symptoms were classified as pelvic or nonpelvic as follows: pelvic symptoms—lower abdominal pain, lower abdominal discomfort or soreness, and leucorrhea; nonpelvic symptoms—headache, nervousness, dizziness, hot flashes, backache, weakness, "high blood pressure," arthritis, precordial pain, indigestion, and urinary symptoms.

Some ovarian tissue was conserved in 111 cases, or 71.6 per cent, and removal of all ovarian tissue or use of radium was carried out in 44, or 28.4 per cent.

Although abdominal pain before, during, and after menstruation or independent of menstruation was the chief symptom in 65.3 per cent of the patients before operation, only twelve complained of abdominal pain and four of abdominal discomfort or soreness in the follow-up series. One required reoperation and this followed a conservative operation in which hysterectomy was not done. In the others who complained of pain, it was not severe or periodic and often occurred only occasionally.

Seventy-nine and three-tenths per cent were well or had nonpelvic symptoms. The results were even better for among those listed as *Improved*, but with some pelvic symptoms, many had only occasional

TABLE II. TYPES OF OPERATIONS AND END RESULTS

OPERATION	NO.	AVER- AGE AGE AT OPER- ATION (YR.)	AVER- AGE TIME OF FOL- LOW- UP (YR.)	END RESULTS				
				WELL	IMPROVED		UNIMPROVED OR DEAD	SUBSE- QUENT OPER- ATION
					PELVIC SYMP- TOMS	NON- PELVIC SYMP- TOMS		
Hysterectomy alone	29	39.40	3.00	13	2	13	1 dead	0
Hysterectomy and bi- lateral oophorectomy	33	39.80	4.40	19	4	10	0	0
Hysterectomy and re- maining ovary	3	34.66	3.61	1	0	2	0	0
Bilateral oophorectomy (no hysterectomy)	3	34.66	7.80	3	0	0	0	0
Radium	5	41.60	5.25	3	1	1	0	0
Hysterectomy and (a) removal of one ovary	52	35.80	3.58	25	14	11	2 died postop- eratively	0
and (b) resection of other ovary	4	30.65	5.64	2	1	1	0	0
Unilateral oophorectomy (no hysterectomy)	16	29.50	5.43	8	5	2	1 unimproved	0
Unilateral oophorectomy and other ovary resected	4	25.25	4.97	4	0	0	0	1
Both ovaries resected	3	26.30	4.58	1	0	2	0	0
One ovary resected	3	27.33	5.28	2	1	0	0	0
Totals	155			81	28	42	Unim- proved 1 Dead 1 Died postop- eratively 2	1

pain or discomfort. Only one patient stated that she was unimproved, and she had had a conservative operation. One patient died of other causes two years after operation.

Conservative Operations

It will be noted that the conservative operations (removal of one ovary and/or resection of ovaries without hysterectomy, were done in 16.8 per cent of the cases, in the younger groups when the disease was not advanced. There were 26 patients in whom pregnancy was possible after conservative operations, of whom 12 were single and 7 remained single. Of the 5 who married later, 3 had children and 2 had no pregnancies. There were 10 women who had had children before conservative operations and none of them had children after operation. But of 4 married women who had no children before operation, 3 had children after operation and one remained sterile. Thus, there is an incidence of 31.6 per cent fertility in the 19 married women who had conservative operations, which may indicate the care in selection of cases for conservative surgical procedures. Of the women who were single at time of operation, one had a small chocolate cyst resected from each ovary and she married later and gave birth to one child and had two miscarriages. In another single patient, thirteen years ago, and therefore not included in the ten-year survey, an adenomyoma

of the left cornu of the uterus was resected because of severe post-menstrual pain. She was married later, and seven years after operation gave birth to a child. With careful selection of cases for conservative surgery the results are not too bad from the standpoint of child-bearing, as Scott⁵ emphasizes. But we believe that the best time for conservatism is before laparotomy is done. Operation should be postponed if possible until the patient has had a reasonable chance to become pregnant for it is doubtful if operation increases the chances of pregnancy.

Ovarian Ablation

Removal of all ovarian tissue, with or without hysterectomy, was done in 39 cases and radium was used in five, an incidence of 28.4 per cent of ovarian ablation. Radium treatment or bilateral oophorectomy was done more commonly in the first five years while hysterectomy alone or hysterectomy with preservation of one ovary or part of an ovary was much more common in the last five years. Conservation of ovarian tissue has been stressed in recent papers by Dannreuther,³ Holmes,⁶ Payne,⁷ Scott,⁵ Haydon,⁴ and Counseller.⁸ As in our series, Holmes⁶ states that hysterectomy with conservation of one ovary was the most frequent type of operation in his series. If both ovaries are hopelessly involved, they are removed. Small chocolate cysts are at times resected leaving sufficient ovary for satisfactory function.

Implants on the pelvic organs or involvement of the bowel wall are not disturbed.

Intestinal Lesions

In the follow-up series there were 17 cases in which at operation definite nodules were found in the wall of the rectosigmoid binding the bowel to the posterior surface of the cervix and uterus. This is a much lower incidence than was found by Jenkinson and Brown¹⁰ who reported 47 cases in a series of 117. These lesions are not disturbed at operation, except to separate them enough to do a subtotal hysterectomy. In only one of them was total hysterectomy done and radium was used in two cases one of which was Case 1, abstracted in this paper. In the remaining 14 cases both ovaries (without hysterectomy) were removed in two, the uterus and both ovaries in four, the uterus and one ovary in six, and hysterectomy alone in two. Ovarian tissue was conserved therefore in eight or one-half of the cases with large bowel involvement. Of the 17 cases, with an average follow-up of six and one-half years, 9 are well and 8 improved, and of the latter only 2 have any abdominal pain. None of the patients have rectal discomfort. The two patients with hysterectomy alone are well. Although the results have been good with preservation of ovaries in our cases with rectal involvement, one hesitates to advocate this procedure in every case, and particularly if intestinal obstruction is imminent, for it may be that total ablation of ovaries gives more rapid subsidence of the lesions. There were many cases with serosal implants on the bowel wall, but only those with definite nodular indurations of the bowel wall are included in this discussion.

Hysterectomy

Hysterectomy with conservation of some ovarian tissue was done in 85 cases, or 54.8 per cent, and in 29 of them the uterus alone was removed. The most prominent symptoms of endometriosis are menstrual (dysmenorrhea, menorrhagia, or irregularity), abdominal pain (usu-

ally worse around time of periods), and dyspareunia. Hysterectomy relieves all menstrual symptoms and it is our experience that the abdominal pain and dyspareunia are relieved also. Clinically the results have been as good as with removal of all ovarian tissue and the menopause was not precipitated suddenly (Case 3).

CASE 3.—Miss F. I., aged 29 years, Elizabeth Steel Magee Hospital, No. 8208. Operation on Nov. 29, 1930 (fourteen years ago and therefore not included in the present survey). Chocolate cyst about 2 cm. in diameter in left ovary. Appendix, right tube, and cystic right ovary had been removed at previous operation. Multiple nodules behind the cervix with one binding the rectum to the cervix. Rectal wall thickened and nodular. Total hysterectomy and resection of chocolate cyst from left ovary, drainage through the vagina. Nine years later patient stated that she had no pelvic symptoms and at no time after operation had she been troubled with hot flashes. On examination a small tender mass was felt in the region of the left ovary.

The end results of hysterectomy for endometriosis compare favorably with hysterectomy for other benign conditions such as fibroids and chronic metritis and indicates subsidence of the active endometriosis.

On the service of a confrere there was a patient who had hysterectomy for endometriosis who later developed a cystic ovary that caused pain enough to finally warrant its removal. It was not a chocolate cyst and no endometriosis was found in the removed ovary. There were no reoperations among the hysterectomy cases in our own series, therefore the opportunity to observe grossly and microscopically what happens to the endometrial implants has been nil.

Conclusions

1. In young women, the surgical treatment of recognized endometriosis should be postponed as long as possible and the decision for operation should be determined by the severity of the symptoms and the extent of the disease.

2. In endometriosis, unrecognized before laparotomy, conservative surgical measures should be used, dependent on the possibility of future pregnancy, the severity of the symptoms, and the extent and location of the lesions.

3. Total ablation of the ovaries in the surgical treatment of endometriosis in women in the menstrual life is not necessary for the relief of this condition, and precipitate menopause is not desired.

4. The removal of the uterus with preservation of uninvolved ovarian tissue is an effective treatment and prevents precipitate menopause.

References

1. Sampson, John A.: *AM. J. OBST. & GYNEC.* 14: 422, 1927.
2. Idem: *AM. J. OBST. & GYNEC.* 40: 549, 1940.
3. Dannreuther, W. T.: *AM. J. OBST. & GYNEC.* 41: 461, 1941.
4. Haydon, G. E.: *AM. J. OBST. & GYNEC.* 43: 704, 1942.
5. Scott, R. B.: *AM. J. OBST. & GYNEC.* 47: 608, 1944.
6. Holmes, W. R.: *AM. J. OBST. & GYNEC.* 43: 255, 1942.
7. Payne, F. L.: *AM. J. OBST. & GYNEC.* 39: 373, 1940.
8. Counseller, V. S.: *AM. J. OBST. & GYNEC.* 37: 788, 1939.
9. Fallas, Roy, and Rosenblum, Gordon: *AM. J. OBST. & GYNEC.* 39: 964, 1940.
10. Jenkinson, E. L., and Brown, W. H.: *J. A. M. A.* 122: 349, 1943.
11. Novak, Emil: *AM. J. OBST. & GYNEC.* 22: 826, 1931.

Discussion

DR. JOSEPH A. HEPP, PITTSBURGH, PA.—Over a period of time we have been interested in ovarian function following hysterectomy. In 1939 we began the study of 39 women who had been hysterectomized in the last ten years. We decided to investigate these patients by three different methods: clinical, histological, and by urinary estrin assays. Our results, with a few exceptions, showed good estrin values when there was no clinical evidence of ovarian decline.

In 1944, fourteen of the original patients returned for further clinical study and hormone assays. One of these patients was extremely interesting in that she had had a hysterectomy in 1939 and an unilateral oophorectomy in 1944. Fifteen assays showed high estrin values, namely, from 30 to 275 I.U. in the interval between operations. The section of ovary, which was recently removed, showed an active corpus luteum with lutein cells and paralutein cells. This patient has been followed for five and a half years and she still experiences a period of depression once a month as she did premenstrually. She is now 36 years old and has not had any menopausal symptoms.

Another patient was studied for a period of eleven years after operation. This patient had one ovary removed at the time of hysterectomy. Assays run six years postoperatively showed high estrin values (125 to 250 I.U.), but assays run recently, eleven years after operation, showed lower values (20 to 55 I.U.). This is interpreted as meaning that the patient has apparently gone through the menopause without any symptoms. Her present age is 50 years. These lower estrin values are similar to the results which we have found in women at the age of 50 years with retained uterus and adnexa.

This entire investigation covered patients between the ages of 25 and 50 years and they were studied three to eleven years after hysterectomy. The amount of ovarian tissue remaining varied from less than one-half of an ovary to two ovaries. Two hundred and seventy-nine estrin assays have been run. The laboratory evidence closely parallels the clinical evidence of ovarian function.

So far we have evidence of normal ovarian function up to eleven years after hysterectomy. The evidence is clinical, histological, and by hormone assays. Our survey is being continued.

DR. JAMES E. KING, BUFFALO, N. Y.—I have always saved a part of an ovary whenever possible in these endometrial conditions of the pelvis. I would like to report in this connection two cases that are of peculiar interest.

One was a young woman about 24 years of age who had bilateral endometrial tumors, on one side about the size of an orange, on the other almost the size of a grapefruit. At operation there were, of course, the usual adhesions, and the larger tumor of the two was removed. On the opposite side the endometrial cyst itself was removed and a very small portion of the ovary was preserved. I brought that together with what I usually call a bundle suture, taking the entire suture around the remaining ovarian tissue. In about a year's time this young woman began to have evidence of hyperplasia, her periods being not only more profuse but more frequent. I curetted and put in 300 milligram hours of radium. About a year after that this patient came to me and said that she had an opportunity to marry. As her periods had returned to normal I advised her to do so but told her that her chances of having a child were negative. She married and in a year's time presented herself and I found her three months pregnant. She had this baby without any difficulty.

The other case was a woman about 35 years of age in whom I removed a large endometrial cyst, and a few points on the other ovary were cauterized where there was evidence of an implantation. I watched this woman, examining her perhaps twice a year. There began to develop on the side on which I had not removed the ovary a tumor which was undoubtedly an endometrial cyst. About

one and a half years later I was called by her physician who said that she had fever and pain in the abdomen which had come on suddenly. We watched her for several days in the hospital. This endometrial cyst that had developed had become infected and formed a very definite anaerobic abscess.

In the second case I have referred to I should possibly have removed the other ovary, but the patient was perfectly comfortable and I had not seen her for a year and a half. I very heartily subscribe to all that Dr. Cashman has said and I think that the removal of both ovaries where a part of an ovary can be retained is too radical surgery. Residual ovarian tissue can always be taken care of later by radium therapy if it indicates any evidence of increase in size.

DR. WM. S. BAINBRIDGE, New York, N. Y.—In 1922 at the meeting of our Association in Albany, New York, I presented a paper on the "Transplantation of Human Ovaries." I had worked with and observed the methods of Professor Tuffier at the Beaujon Hospital in Paris and then carried on his methods in America. Success depends on a number of factors:

1. Cut away all diseased tissue, retaining only that which is normal.
2. Handle the tissue to be transplanted with meticulous care, in order not to injure it.
3. Insert the graft in a pocket behind the right or left rectus muscle on the deep epigastric artery and veins—preferably the raw surface of the transplant—in close proximity to the vascular radicals, where traumatism is less likely to occur.
4. No matter with what care the foregoing is carried out, failure will result unless ovarian hormone, either by hypodermic or ingestion, is started a day or two after the operation and continued for from four to six months. This allows time for vascularization of the graft to be re-established instead of the graft's being absorbed by Nature's effort to get the endocrine it needs. With Tuffier I inspected some of his transplanted grafts in the abdominal wall, and noted Graafian follicles from one to four years after the operation, showing that the gland was functioning.

Many of my cases have returned to me some months and even years after the operation, complaining of symptoms each month of normal menstrual cycle—swelling of neck and breasts, and pain where the transplant was situated.

DR. CASHMAN (closing).—I was particularly interested in the report of Dr. King's patient where he resected a chocolate cyst and the patient afterward became pregnant in spite of the fact that he used radium to stop some of the flow.

The use of ovarian grafts is a valuable procedure. We have a series of patients who continue to menstruate if we remove both ovaries and implant segments of the ovary in the rectus muscle.

SURGICAL COMPLICATIONS DURING PREGNANCY AND LABOR*

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THE pregnant woman is subject to the same surgical lesions as the nonpregnant patient and, in many instances, the complication of pregnancy makes little, if any, difference in the management of her case. Fractures and other traumatic injuries, for instance, have no obstetric significance. Others, such as hemorrhoids and varicose veins, are more common during pregnancy but require only simple instruction, or occasionally a minor surgical procedure, such as the opening of a thrombosed hemorrhoid under local anesthesia. In cases of otitis media, unless acute, most hernias, and other conditions of no immediate urgency, operation is best deferred until after confinement.

Another group of patients are those in whom the pregnancy itself requires surgical treatment. These comprise abortions, ectopic gestations, accidental hemorrhage, placenta previa, rupture of the uterus, and cesarean section. These conditions would each warrant a separate discussion and will not be treated in this paper, which will be confined to a consideration of those surgical conditions where pregnancy complicates the diagnosis and treatment. It is difficult for an obstetrician to be dogmatic regarding the proper conduct of many surgical conditions, and the views here expressed are the impressions that have resulted from a study of the histories of the surgical conditions complicated by pregnancy in this hospital during the past eight years. Many of these patients were seen in the obstetric and gynecologic services; the remainder were admitted to the surgical services, and my knowledge of them, for the most part, is derived only from a study of their histories. The discussion will be divided into gynecologic conditions during pregnancy and general surgical conditions in the pregnant woman.

Fibroids and Pregnancy

Autopsy statistics indicate that about 20 per cent of women beyond the age of 35 have fibroids, yet these tumors are reported in only approximately 1 per cent of pregnant women. It would appear, therefore, that many of the smaller tumors are unrecognized during pregnancy. It is also a fact that the incidence of sterility is increased in women with fibroids. Their presence materially increases the inci-

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dence of abortion, miscarriage, premature labor, dystocia, and post-partum hemorrhage. Because of their tendency to cause sterility and to result in complications during pregnancy, myomectomy may be advisable when sterility is the only indication. In many cases the first subsequent pregnancy may result in abortion or miscarriage. Small tumors discovered during pregnancy are usually of little significance, and even large tumors may not seriously interfere. Size alone may be an indication for myomectomy, and this is particularly true in the first pregnancy. In such cases, myomectomy done before complications have developed may result in a miscarriage but will leave a uterus capable of future pregnancies, whereas operation required later in pregnancy may demand hysterectomy as well as the loss of the pregnancy. All cases of degeneration of fibroids during pregnancy do not require surgical treatment, for the process frequently becomes quiescent under conservative management and the pregnancy may go to term. Torsion of a pedunculated tumor requires immediate operation.

TABLE I. FIBROIDS AND PREGNANCY

Number of cases	51
Operation during pregnancy	17
Operation at labor	3
Palliative treatment	31
Myomectomies	8
Confined at term	5
Aborted	1
Died (pulmonary embolism)	1
Cesarean section and myomectomy	1
Hysterectomies	12
During pregnancy	10
At labor	2
Palliative treatment	31
Delivered at term	22
Aborted	9

In the series under study there were 51 cases in which fibroids were discovered in pregnant women. Of these, 17 required operation during pregnancy, 3 were dealt with at the time of labor, and 31 did not require treatment but only palliative measures.

Seven of the seventeen patients requiring surgical treatment during pregnancy were treated by myomectomy; five of these were subsequently confined at term; one had an incomplete abortion and was curetted at the time of the myomectomy; and one died of pulmonary embolism following operation. Ten patients were treated by hysterectomy for various reasons. One patient, aged 40, with two children, had a large tumor and had severe pain and slight bleeding when four weeks pregnant. Under expectant treatment the symptoms disappeared but recurred a month later. The bleeding was so severe that it was felt the pregnancy would not go to term. The second patient, para ii and six months pregnant, had multiple fibroids, was bleeding freely and having pains at the time of operation. The third patient,

a primipara, was six weeks pregnant and had a mass of fibroids rising to the umbilicus and was suffering from severe pressure symptoms. She had two cervical tumors and dense adhesions from a previous appendectomy. Myomectomy was attempted in one case, in which a large tumor had undergone degeneration when the patient was six weeks pregnant, but bleeding at the time of operation necessitated hysterectomy. The fifth patient, para ii, had a large cervical fibroid and signs of inevitable abortion. In the sixth patient bleeding had been present for three weeks, after which pain developed. Hysterectomy was done because of the position of the multiple fibroids. The seventh patient had four living children, an early pregnancy, and active pulmonary tuberculosis. In two cases the patients stated that they had not missed a period and early pregnancy was discovered only after the specimens were opened in the pathologic department. The last patient had four children and had acute degeneration of a large tumor when three and one-half months pregnant. She was treated expectantly but did not respond.

There were three cases in which treatment was called for at the time of labor. The first patient was a primipara at term with a tumor in the pelvis which could not be dislodged by manipulation. She was delivered by cesarean section and a myomectomy was done. The second patient was also a primipara at term; a large cervical fibroid filled the pelvis and a cesarean section and hysterectomy were done. The third patient had had a myomectomy before marriage and had gone to term in her first pregnancy but was delivered by cesarean section because of disproportion. She subsequently developed another fibroid the size of a large orange. This pregnancy also went to term, and after delivery by section a hysterectomy was done.

Thirty-one patients did not require any surgical treatment during pregnancy and labor. Nine of these aborted spontaneously; one of these had previously been delivered at term, and another went to term in a subsequent pregnancy. Twenty-two patients had no untoward symptoms during their pregnancies and were confined at term. In one of these, death of the fetus had occurred in utero, thirteen had normal deliveries, and nine were delivered by forceps. Six that went to term had symptoms of degeneration, which responded to expectant measures. One patient, after a normal delivery, had a postpartum hemorrhage which was followed by irregular bleeding in the puerperium. Of the thirty-one patients treated expectantly, five had tumors as large as, or larger than, a small grapefruit.

It is interesting to note that of the fifty-one cases, thirty-two fibroids were discovered during the patient's first pregnancy, seven during the second pregnancy, eight during the third pregnancy, and four during the fifth pregnancy. Two of the latter had had stillborn children. It is very probable that many of the primiparous patients will eventually require surgical treatment for the fibroids. It is also interesting

to note that only one of the patients suffered from postpartum hemorrhage and that one required manual removal of the placenta.

Ovarian Tumors and Pregnancy

Ovarian tumors complicate pregnancy less frequently than do fibroids, but conservative measures play a smaller role in their treatment. It is true that with small tumors there may be a doubt whether they are simply retention cysts or neoplasms, and such tumors, if they do not increase in size, may be left alone until after delivery. The danger of malignancy in younger women is slight, particularly in the case of small tumors. The possibility of twisted pedicle, however, is greater with the smaller sized tumors, and in those cases treated expectantly this danger must always be kept in mind. Large ovarian tumors should always be removed because of the inevitability of distressing pressure symptoms as the uterus enlarges and because of the danger of complications such as pressure necrosis, hemorrhage into the tumor, interference with delivery, and malignancy. Borderline tumors, larger than a small grapefruit, are better removed, but, if possible, operation should be delayed until after the end of the third month. At operation, the uterus and the opposite ovary should not be handled. If the corpus luteum of pregnancy is incorporated in the tumor, the post-operative administration of progesterone has been advocated as a prophylaxis against abortion, but even when this is not given many pregnancies go to term. An ovarian tumor with a twisted pedicle is an acute surgical emergency demanding immediate operation. If an ovarian tumor is first discovered during labor and lies above the pelvic brim or can be displaced to such a position, labor should be allowed to proceed. The danger of a twisted pedicle, however, remains throughout the puerperium, and operation should be carried out as soon as any symptoms arise.

TABLE II. OVARIAN TUMORS AND PREGNANCY

Number of cases (all operated upon)	16
Dermoids	3
Brenner tumors	1
Retention cysts	1
Cystadenomas	11
Course of pregnancy	
Abortion	3
Premature labor	1
Term	12
Size of tumor	
Small (both twisted pedicles)	2
Medium (four twisted pedicles)	8
Large (one aborted)	6

There were sixteen patients with ovarian tumors in this series. Ten were in the first pregnancy, two in the second, two in the third, one in the fifth, and one in the sixth pregnancy. All of these patients were

operated upon. One patient was seven months pregnant at the time of operation for bilateral dermoids; one tumor had a twisted pedicle. She came in labor a few days later, and the baby survived. A second patient was suffering from inevitable abortion at the time of operation for a large tumor filling the pelvis, and a curettage was done at the time the cyst was removed. Two other patients aborted, one three and the other twelve days after operation. The remainder of the patients were delivered at term. Torsion of the pedicle had occurred in six patients, in one of which the preoperative diagnosis was acute appendicitis. Eight patients had no symptoms referable to the tumor. The remaining two patients complained of pain and bleeding; one went to term and the other aborted, as noted. Eight patients were operated upon after they had passed the third month of the pregnancy; one of these aborted and one went into premature labor. In the other six, the pregnancy was not disturbed.

The size of the tumors was of some interest. In two patients the tumors were small but had twisted pedicles. One of these patients went to term, and the other had premature labor. Eight patients had medium-sized tumors, of which four had twisted pedicles, and two of these patients aborted. Six patients had large tumors, none of which had twisted pedicles, and one abortion followed operation in this group. Three of the sixteen tumors were dermoids, and one was a Brenner tumor.

TABLE III. POTASSIUM PERMANGANATE BURNS

Number of cases	32
Not pregnant	4
Aborted in hospital	8
Aborted later	4
Confined at term	16
Treatment	
Palliative	17
Packing	11
Ligature	4

We frequently see patients in our clinic bleeding from the vagina after the insertion of a potassium permanganate tablet in an attempt to induce abortion. It appears to be a growing belief that this is an efficient method of producing abortion. In most cases the insertion of the tablet is followed by bleeding from the resulting ulceration, and this bleeding is interpreted by the patient as abortion, and, therefore, it is difficult to convince women of its danger and uselessness. Potassium permanganate tablets can be bought without a physician's prescription. There were thirty-two of these patients in our wards in the last five years. Of these, four were not pregnant at all; eight of them aborted while in the hospital; four left the hospital and subsequently aborted and returned to hospital; sixteen of the patients went to term, some of them in spite of severe hemorrhage. Six patients required

transfusions and all of these went to term. In seventeen the bleeding had ceased either before the patient entered the hospital or shortly afterward and required only palliative treatment.

Many of these patients denied having attempted to produce abortion, but inspection with the speculum revealed the characteristic punched-out ulcer, surrounded by a deep purple stain, which, once seen, cannot be mistaken.

Cancer of the Cervix Complicating Pregnancy

The cancer clinic of the Toronto General Hospital treats about eighty new cases of cancer of the cervix each year, and during the past ten years only four cases have been complicated by pregnancy. One of these patients was a woman 32 years of age, who entered the hospital because of an incomplete abortion, and at the time of the curettage an early carcinoma was discovered. One patient, four months pregnant, had a stage 2 carcinoma of the cervix. The uterus was emptied by supravaginal hysterotomy and the cancer treated by the usual radiologic methods. Two patients were discovered to have carcinoma after delivery, one from our wards and one from another city. The first, aged 40, para v, had an early carcinoma. Notwithstanding treatment by high voltage and radium, she died in three years. The other was aged 33, and the cancer was discovered eight weeks after her seventh confinement. She now has no clinical evidence of the disease three years after radiologic treatment. On the basis of this meager experience, it is difficult to justify any dogmatic opinion, but in general it is our view that if the pregnancy is near term treatment can be delayed in the interests of the child, but in other cases the pregnancy should be terminated immediately after the diagnosis is made. Abdominal hysterotomy is the method of choice. The carcinoma is then treated by high voltage therapy followed by the use of radium.

Vaginal Cysts Complicating Pregnancy and Labor

Apart from small inclusion cysts near the introitus, the common cystic tumor of the vagina arises from remains of Gartner's duct. The cyst is usually thin walled and flaccid and frequently is not discovered during pregnancy. With the onset of labor and the descent of the presenting part, the fluid in the upper part of the tumor is forced down and may present as a mass sufficient to encroach seriously upon the diameter of the vagina. By displacing the presenting part and putting pressure upon the tumor, its contents can again be forced above the presenting part, which will then descend normally. We have encountered five patients with such tumors, and the suggested procedure was successfully carried out in four of them. In the fifth it was necessary to evacuate the contents of the tumor with a syringe.

General Surgical Conditions Complicating Pregnancy

As previously stated, it is our intention to discuss only the more serious surgical complications of pregnancy. In reviewing the surgical conditions, however, it was a matter of surprise to discover how many operations of election were carried out on patients who were pregnant. It was equally a matter of surprise to find how infrequently abortion followed such surgical procedures. A striking example of an extensive surgical procedure is that of the patient, four months pregnant, who developed a pulmonary abscess in the lower left lobe. A lobectomy was done and the patient was successfully delivered at term. A list of operations on pregnant patients during this period includes nephrectomy, removal of a fibromyoma of the jaw, removal of several nonmalignant tumors, two herniotomies, operations for osteomyelitis, open reduction of fractured long bones, tonsillectomies, and operation for mastoiditis.

Appendicitis.—Appendicitis is by far the commonest indication for an operation of necessity during pregnancy, although the incidence of the disease is probably no greater during pregnancy than at any other time. There seems to be little doubt that acute appendicitis during pregnancy is a somewhat more serious condition than in the nonpregnant patient, and the seriousness increases considerably when the uterus has risen above the pelvic brim. The localization of the inflammatory process tends to be interfered with and the probability of general peritonitis is increased. The necessity of correct diagnosis and early operation is, therefore, particularly desirable, but the great difficulty appears to lie in making a correct diagnosis. This, of course, also applies to the nonpregnant patient, but there are certain pitfalls in diagnosis during pregnancy. Keeping in mind these special difficulties, to which reference will be made later, operation is the safest procedure when the symptoms and findings strongly indicate a probable acute appendicitis, even though the removed appendix is subsequently found to be not acutely inflamed.

TABLE IV

Operations during pregnancy (6 aborted)	18
Operations after labor (1 death)	2
Pathologic Reports	20
Acute appendicitis	8
Chronic appendicitis	8
Normal appendix	1
Twisted ovarian cyst	1
Acute salpingitis	1
Attempted abortion	1
Cases not operated	24
Diagnosis not confirmed	11
Becoming quiescent	3
Diagnosis changed	10

There were forty-two pregnant patients sent to the hospital with a diagnosis of acute appendicitis. In twenty-one of these the diagnosis was concurred in after admission, although in one patient a diagnosis of pyelitis of pregnancy at seven months was first made, and three days later it was necessary to do an emergency operation, when a gangrenous appendix was removed. The patient went into labor prematurely and developed general peritonitis but eventually recovered. Eighteen of the twenty-one patients with a diagnosis of appendicitis were operated upon, and following operation six abortions occurred. There were no deaths. Only six of the eighteen patients operated upon were reported as having acute appendicitis by the pathologic department; eight were reported as having chronic appendicitis, although in one of these the appendix was engorged with pinworms. One was reported as having a normal appendix. Incorrect diagnosis was made in three of the eighteen patients operated upon. One had a small ovarian cyst with a twisted pedicle; one had an acute salpingitis early in pregnancy; the third patient was a widow who gave a history of normal periods and denied the possibility of pregnancy even after operation. Her symptoms were due to taking drugs with the idea of causing abortion. She did not abort, even after operation. The diagnosis was not confirmed in eleven of the twenty-four patients not operated upon. The majority of these patients had some pain in the lower right abdomen and were sent to the hospital with a tentative diagnosis of appendicitis, but as no other evidence of the disease could be discovered, and the pain quickly disappeared, the diagnoses were simply listed as "not confirmed." Three patients were thought to have had acute appendicitis but were definitely becoming quiescent at the time of admission and were treated expectantly, with the advice that the appendix should be removed after delivery. In ten patients other diagnoses were made. One was the vomiting of early pregnancy, one was diagnosed "hysteria," and one was pyelitis of pregnancy. Seven patients presented difficulty in diagnosis because of attempts to produce abortion by medicinal or other means and concealed this information. The possibility of error in diagnosis in these cases is great. The patients complained of low abdominal pain, often confined to the right side, which was frequently accompanied by nausea and vomiting. When mechanical means were employed to produce abortion, abdominal tenderness and rigidity were sometimes present and also some degree of fever and leucocytosis. Abdominal tenderness may also be present when intestinal irritants have been taken. Apart from attempts to produce abortion, the vomiting of early pregnancy is not infrequently accompanied by localized abdominal pain.

In addition to these cases of appendicitis during pregnancy, two patients developed acute appendicitis during labor. In both instances the diagnosis was missed during the process of parturition, but one

case was recognized a few hours after delivery and the patient was successfully operated upon. The second case was not recognized as an acute appendix until the third day after delivery, and by the time the operation was performed the appendix had ruptured and a general peritonitis had developed. This patient died.

Intestinal Obstruction.—Intestinal obstruction occurring during pregnancy presents many difficulties in diagnosis, and the delay in operation due to these may prove fatal. The obstruction is usually secondary to pre-existing adhesions, and the danger of its occurrence is accentuated by the mechanical effects of the enlarging uterus. It sometimes arises when no previous operation has been performed and, in these cases, a history suggestive of appendicitis or a previous pelvic inflammation may be obtained. The difficulty in diagnosis is due to the fact that the classical symptoms of cramplike abdominal pain and vomiting are not infrequently seen in normal pregnancy. After delivery, either normal or operative, ileus occasionally develops, and the marked distention is sometimes mistaken for mechanical obstruction. Such cases of ileus may be accompanied by vomiting, but cramplike abdominal pain is usually absent. It sometimes requires great clinical acumen to avoid operating upon nonobstructive ileus and to operate early when true obstruction exists.

TABLE V. INTESTINAL OBSTRUCTION

Number of cases		7
Number of operations		6
Carcinoma of the sigmoid	2	
Adhesions	2	
Strangulated umbilical hernia	1	
Postoperative obstruction	1	
Treated expectantly		1

In this series there were seven cases of intestinal obstruction during pregnancy. Two were due to carcinoma of the sigmoid. One of these was in a woman 42 years of age and a colostomy was done. She was seven months pregnant in the fourth pregnancy and had a premature labor. She survived the operation but died in two months. The other patient was 32 years of age and was seven and one-half months pregnant in the first pregnancy. Medical induction was done before operation and a live baby obtained. The patient was operated upon two days after delivery and died the following day. Two cases were due to adhesions. One patient was four months pregnant and subacute obstruction from a previous appendectomy was diagnosed. At operation many adhesions were encountered but no acute bowel obstruction. The patient was delivered at term. The other patient had an acute small bowel obstruction due to adhesions following a previous operation for ovarian cyst. She was operated upon when four months pregnant in the second pregnancy and the obstruction was relieved.

She was subsequently confined at term, and a month later developed a volvulus which required intestinal resection. In the fifth case, the patient was six months pregnant in the fifth pregnancy. An umbilical hernia had been present for several years and became strangulated with symptoms of obstruction. At operation strangulated omentum only was encountered. The patient was delivered at term. The sixth case was of unusual interest. The patient entered the hospital when three and one-half months pregnant with general peritonitis. A month previously she had been in the hospital with a potassium permanganate burn. When operated upon for general peritonitis, the right tube and the appendix were both removed, but it could not be decided whether the peritonitis was secondary to the previous permanganate lesion or to an acute appendicitis. Three weeks after the primary operation she developed acute intestinal obstruction requiring a second operation, following which she aborted. After a stormy convalescence, she recovered. The last patient had had seven pregnancies, the last of which had been at term five months previously. She was again two months pregnant and was sent to the hospital with a diagnosis of acute obstruction. The symptoms, however, subsided under expectant treatment; the patient was not operated upon and went to term. This case was probably not one of intestinal obstruction although it was so diagnosed. Although no history of interference could be obtained, it was more probably the real cause of her symptoms.

Hyperthyroidism During Pregnancy.—Some enlargement of the thyroid gland occurs in nearly a third of all pregnant women. This, in addition to the frequent nervous instability of pregnancy, often accompanied by tachycardia, may rouse the suspicion that hyperthyroidism is present. The true diagnosis is made more difficult by the fact that the basal metabolic rate is often raised during pregnancy. Baer's study showed forty-four normal women with basal metabolic rates of plus 30 to 55 during the last trimester of their pregnancy. Some observers maintain that pregnancy does not alter the course of exophthalmic goiter, while others believe that pregnancy tends to aggravate its course. Hyperthyroidism accompanies two distinct types of thyroid disease: diffuse hyperplasia of the gland (exophthalmic goiter) and nodular hyperplasia. In the former, remissions are not uncommon, although recurrent exacerbations are the rule, any one of which may proceed to a thyroid crisis. On the other hand, an adenomatous goiter with toxic symptoms usually becomes progressively worse, and the effect of iodine therapy is not only uncertain, but transitory at best. Those observers who believe that hyperthyroidism is frequently made worse by pregnancy advocate the emptying of the uterus. It is our opinion, however, that therapeutic abortion is not indicated in these patients, and the hyperthyroidism should be treated appropriately without regard to the pregnancy. When operation is indicated,

it may be carried out with little, if any, greater risk than in the non-pregnant patient. On the other hand, if a patient with exophthalmic goiter responds to medical treatment, and the pregnancy is advanced, it is probably best to delay operation until after delivery.

TABLE VI. HYPERTHYROIDISM

Number of cases	9
Number of operations	3
Number of abortions	0
Simple colloid goiter	5
Hyperplasia due to pregnancy	1
Toxic adenoma (operated)	2
Exophthalmic goiter (operated)	1

There were nine cases in this series in which the patients were admitted to the hospital with a diagnosis of hyperthyroidism during pregnancy. Of these, five diagnoses at the hospital were simple colloid goiter, the symptoms being interpreted as the result of pregnancy. They were all treated expectantly, and all went to term. Three of the patients were in the first pregnancy, one in the sixth, and one in the eighth. One woman, who was three and one-half months pregnant, had a goiter with suggestive symptoms. It was decided, however, that the goiter was a hyperplasia due to pregnancy. She was not operated upon and went to term. Three cases were true toxic goiters, one being an exophthalmic goiter, and the other two toxic adenomas. These patients were three months, five months, and seven months pregnant, respectively. Two of them were primiparas and the third was in the fourth pregnancy. All three patients were operated upon and in no case did miscarriage occur. Two of them had a very stormy convalescence, but all three recovered.

Summary

1. When fibroids complicate pregnancy, conservatism in treatment is usually indicated.
2. Ovarian neoplasms usually require operation during pregnancy.
3. Correct diagnosis of appendicitis during pregnancy is frequently difficult.
4. Symptoms due to the pregnancy or to attempts to produce abortion may lead to erroneous diagnosis. A large percentage of pregnant patients sent to hospital because of acute appendicitis do not have the disease.
5. In the treatment of hyperthyroidism and pregnancy the following points are important: (a) Is hyperthyroidism really present? (b) If so, is the condition an exophthalmic goiter, or a toxic adenoma? If the former, conservative treatment will often be satisfactory, but if toxic adenoma is present, surgical treatment is indicated.

Discussion

DR. FREDERICK H. FALLS, CHICAGO, ILL.—We note in general a thread of conservatism running through the management of these cases which we highly approve. We see also a willingness to accept the responsibility of performing an unnecessary operation when the diagnosis was in doubt in order to safeguard the patient from the risk of development of lesions so far advanced as to be beyond surgical remedy. In this viewpoint we also concur.

We would like to stress the value of corpus luteum extract injections as a prophylactic measure to avoid abortion in all of these surgical complications of pregnancy. We would also suggest that it would be for the benefit of all concerned if all surgical procedures of pregnant women have the benefit of obstetric consultation before surgical treatment is applied. This would result in a better understanding of these relatively rare complications by the surgeon and the obstetrician and better treatment for both mother and baby.

With regard to ovarian tumors we tend to conservatism unless there is evidence of rapid increase in size or twisting of pedicle either ante or post partum. During labor, if cysts block the inlet paracentesis may be employed for decompression.

For cervical carcinoma, if operable, hysterectomy should be done regardless of the pregnancy, followed by x-ray and radium. It is a rare condition but probably not as rare as Dr. Scott's figures would indicate. For years no case of this kind was diagnosed at the Cook County Hospital in Chicago. In the last two years eight cases were recognized because the staff had become conscious of the possibility of such complications. It is significant that two of these cases were not discovered until after delivery. This means that either the patients were not examined by the obstetrician attending the case or they were not recognized as carcinomas when seen because of the rarity of the lesion. How can we diagnose an early carcinoma of the cervix without a vaginal examination and careful inspection of the cervix with a good light, followed by biopsy in suspected cases?

In handling vaginal cysts we would evacuate with a syringe at labor and dissect out later.

In 44 patients with a tentative diagnosis of appendicitis only twenty were operated upon and ten proved to have acute appendicitis at operation. These figures illustrate the desirability of a conservative attitude. When, however, the pregnant woman develops the symptoms of acute appendicitis in sequence, as pointed out by Dr. J. B. Murphy, pain diffuse then local, nausea and vomiting, chill, leucocytosis, right rectus rigidity, operation should not be deferred. It is well to remember that after the fifth month the pain and tenderness are not over McBurney's point but higher due to upward displacement of the appendix unless bound down by adhesions following previous attacks.

In three of seven cases so diagnosed the patients did not have intestinal obstruction. In the first case of carcinoma of sigmoid, careful management of the bowel might have permitted the patient to go to seven and one-half months or longer, when induction might have saved the baby. With a tumor developed to this degree the outlook for the mother is poor and delay of operation for a few weeks to give the baby a better chance is justifiable.

There is almost always some hyperthyroidism during normal pregnancy as shown by increased size of the gland and increased basal metabolic rate and other symptoms of hyperactivity of the thyroid gland. This is physiologic and desirable. When this increase of gland activity goes beyond the physiologic limits, toxic symptoms may demand treatment. Bed rest and Lugol's solution are all that are necessary in the great majority of cases. This may be continued

for weeks during pregnancy, the opinion of many thyroid surgeons to the contrary notwithstanding.

Following labor, which is usually very well tolerated, the acute symptoms of hyperthyroidism usually subside and operation is not necessary. We have not had to operate upon a single patient before the termination of pregnancy. Pregnancy in the woman who has previously been operated upon for hyperthyroidism may be a complicated therapeutic problem. Such patients may become very nervous following delivery of the baby and in one of my patients suicide resulted.

I would disagree with Dr. Scott in the statement that fractures and other injuries have no obstetric significance, and I assume that he did not mean this statement to be taken literally. For example, abortion is certainly predisposed to and rupture of the uterus has been ascribed to violent trauma. There is some evidence to show that fractures do not always heal as well as in the nonpregnant woman, which may be due to altered calcium metabolism during gestation.

Varicose veins may become thrombosed and may predispose to pulmonary embolism either ante partum or post partum.

As mentioned, about 20 per cent of women beyond 35 years have fibroids, but relatively few of these become pregnant. Women under 25 years rarely have fibroids of sufficient size to influence the course of pregnancy and labor. In our experience 40 per cent of the cases needing surgical intervention is too high, but the indications given in the cases here reported seem entirely justified. Myomectomy is especially adapted to subserous variety. In cases of sterility with submucous fibroids, abdominal hysterotomy should be done. In such cases, if pregnancy results, cesarean section is advisable, especially if the patient is an elderly primipara.

DR. WILLIAM H. VOGT, St. Louis, Mo.—A matter that interested me was the handling of a case of carcinoma of the cervix associated with pregnancy. Dr. Scott said that the desirable thing to do in late pregnancy is to wait for a short time, do a section, and then treat the cervical stump with radium. In the early cases he advises the emptying of the uterus, preferably by hysterotomy, and then treating the case in the usual manner with radium. In a Catholic hospital where I work you cannot empty a uterus for a pregnancy associated with a carcinoma, but you are permitted to take out that uterus. If it is not an operable case, we would ordinarily use radium, but this would probably produce an abortion.

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—I shall attempt to answer the question of Dr. Vogt because I, too, work in a Catholic hospital. In a case of carcinoma of the cervix complicating pregnancy, we are permitted, as Catholics, to treat the carcinoma. If it is before the period of viability, we may use x-ray therapy applied externally because we are not attempting to destroy the innocent victim but are treating the carcinoma. If the fetus is viable, we remove the pregnancy by cesarean section, which is permissible, and then treat the carcinoma either by total removal of the uterus or by leaving the uterus behind. If the uterus is left behind, we may begin external irradiation two or three days postoperatively, sterilize the carcinoma as much as possible before the insertion of radium, which should not be done before complete involution has taken place.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—In March a DPA case was brought in to us, a para vii, who had been in labor under the care of a midwife for four days. Examination showed a very extensive carcinoma of the uterus and a dead fetus. A classical cesarean section was done. It was found that the base of the bladder and the sigmoid were incorporated into a malignant mass so that one could not even attempt a hysterectomy. A drain was put in on each side of

the uterus, the patient was given three transfusions of bank blood and deep x-ray therapy started ten days after operation. Six weeks later this patient was able to walk out of the hospital. The drainage had stopped and the abdominal wound was closed. She went home to the country and she is still alive.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—I can agree very fully with all the principles enunciated in the paper except in regard to the treatment of fibromyomas during pregnancy. Although we have many cases of fibromyomas complicating pregnancy in our part of the world, we have not done a myomectomy during pregnancy for over twenty-five years except in cases of acute necrosis and in one or two cases where the abdomen was opened in error and the fibromyoma exposed. Ordinarily we do not do a myomectomy at the time of cesarean section unless there is some real indication for it because of the risks of additional serious hemorrhages and of disseminating potentially infected fluids and clot. Unless there is a real indication for myomectomy, we prefer to treat cases of fibromyomas by hysterectomy, unless we want to preserve the uterus for future childbearing. Myomectomy for multiple or large fibromyomas is frequently justifiable and should be done without hesitation in cases of sterility in which the tumor is considered as a potential factor in the sterility. As a general rule, fibromyomas which are not giving rise to symptoms are merely kept under periodic observation, operation being resorted to only for specific indications. Complete or supravaginal hysterectomy is usually selected on the basis of the condition of the cervix and of the factor of added risk involved in cases of technical difficulty in the performance of complete hysterectomy.

DR. SCOTT.—I believe if a patient with cancer of the cervix and a non-viable child came under my care, and I was allowed to remove the uterus, I would do so by subtotal hysterectomy. Our treatment of cancer of the cervix begins with deep x-ray therapy lasting four to eight weeks, after which radium is applied. It is my opinion that in such cases there is no advantage in doing an ordinary total hysterectomy in place of a subtotal.

Regarding our myomectomies, seven were done during pregnancy and one at the time of labor. Some of these had undergone degenerative changes which did not respond to treatment; in other cases it was our opinion that the size or position of the fibroid made operation advisable during the pregnancy.

As to the importance of surgical consultation, I agree most decidedly. The closer cooperation between the general surgeon and the obstetrician and gynecologist, the better for both. There was a time when many surgical and some medical conditions were found to be complicated by pregnancy, that the opinion of the obstetrician was sought solely on the question of whether or not the uterus should be emptied. This, in general, is no longer true.

PREGNANCY FOLLOWING MYOMECTOMY*

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FIBROMYOMAS of the uterus requiring treatment frequently are encountered in nonpregnant women of the childbearing age, and occasionally it becomes necessary to treat such tumors surgically in the course of pregnancy. If one could disregard the childbearing function of the uterus among the former group of patients and the presence of pregnancy in the latter, the problem of treatment in the majority of cases would be solved by the performance of hysterectomy or by the use of irradiation. However, in many cases of fibromyoma of the uterus it is highly desirable to conserve the reproductive function by avoiding the employment of these measures, if this is consistent with the relief of symptoms and with sound surgical judgment. In employing such conservative treatment one must be mindful that the tumor may be unrelated to past or possible future infertility and that myomectomy may not influence favorably the patient's obstetric future. Subsequent to myomectomy, symptoms may occur or myomas may reappear and require surgical treatment or irradiation; also, because of the nature of the operation, complications occasionally may develop as they did in four of the cases which we shall consider. Such complications are less likely to occur after hysterectomy.

Interest in these considerations led us to review a group of cases in which women less than 45 years of age had undergone abdominal myomectomy. We selected 250 cases in which myomectomy was performed between Jan. 1, 1925, and Dec. 31, 1940, inclusive. In all of the selected cases, the patients had been married more than three years and previously had not received treatment which would decrease their fertility. No case was included unless one or more myomas of 1 cm. or more in diameter were imbedded in the uterine wall. No case of adenomyoma was included.

In twenty-nine of the 250 cases, the patients were pregnant when the myomas were found. Tubal pregnancy was present in four of the twenty-nine cases and myomectomy was performed at the time of tubal resection. In two cases cesarean section and myomectomy were performed at term. In the remaining twenty-three cases myomectomy was performed in the course of intrauterine pregnancy. In two of these cases, the fetus was removed by hysterotomy in the course of

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extensive myomectomy. In seven cases spontaneous abortion occurred after myomectomy. In two cases premature labor occurred and the infants died. In the twelve remaining cases the pregnancy continued to full term. In two of these cases the infants died. One of these deaths was due to hydrocephalus and the other was due to birth trauma.

Fetal mortality is high in cases in which myomectomy is performed in the course of intrauterine pregnancy. In the twenty-three cases just mentioned and in two cases in which cesarean section and myomectomy were performed at term, twelve infants survived.

In sixteen of the twenty-nine cases in which the myomas were found in the course of pregnancy, the patients subsequently became pregnant and gave birth to twenty-three children.

One of us (R. D. M.) and Hardwick¹ reviewed thirty-two cases in which myomectomy was performed in the course of pregnancy at the Mayo Clinic and found that abortion or premature labor occurred in fifteen of the cases. Pierson² reported that abortion or premature labor occurred in 24.1 per cent of 250 cases in which myomectomy was performed. Counseller and Bedard reported similar results.³

Few complications occurred in the twelve cases in which intrauterine pregnancy continued to full term after myomectomy was performed at the clinic. Persistent "spotting" occurred in one case. Cesarean section was performed in one case because of heart disease. Spontaneous delivery occurred in seven cases. In one case in which the child was delivered through the vagina, the placenta had to be removed manually.

The indications for operation were as follows: Four of the twenty-nine patients were operated on because of ectopic pregnancy. In seventeen cases operation was performed for a tumor in the pelvis associated with pregnancy. In three of the seventeen cases the pregnancy was not diagnosed before the operation. Four patients had symptoms caused by degeneration of the fibroids. Uterine bleeding occurred in one case. In one case operation was performed for an ovarian cyst with a twisted pedicle and uterine myomas. As stated previously, in two cases myomectomy and cesarean section were performed at full term.

In eighty-two of the 221 cases in which the patients were not pregnant when myomectomy was performed, there was a history of infertility prior to the operation. Eight of the patients subsequently conceived twelve times (one set of twins) and gave birth to a total of eleven living children.

In seventy-six (30 per cent) of the entire series of 250 cases, significant evidence of myomatous changes in the uterus occurred after myomectomy. In fifty-one of these cases some form of treatment was necessary. Surgical treatment was employed in forty-two cases and irradiation was used in nine.

One hundred one of the 250 patients became pregnant 167 times after myomectomy. One patient became pregnant six times, two became pregnant four times, fifteen became pregnant three times, twenty-five became pregnant twice, and fifty-eight became pregnant once. In these 167 pregnancies there were thirty-one abortions, one ectopic pregnancy, three stillbirths, four neonatal deaths, and 128 surviving infants, one of whom was premature. One of the neonatal deaths occurred at the twenty-sixth week of gestation; one occurred in a case of placenta previa and one occurred in a case of premature separation of the placenta. In the remaining case the cause of death was not determined.

In five cases persistent spotting of blood from the vagina occurred during pregnancy. In two of these cases there was great irritability of the uterus which was accompanied by cramping; in all of these cases the pregnancy continued to term. Premature labor occurred in two cases, placenta previa in two, delayed postpartum hemorrhage in two, and premature separation of the placenta, ectopic pregnancy, and circumvallate placenta in one case each. Cesarean section was performed thirteen times. In five cases it was performed because of the presence of fibroids; in one of these cases a Porro operation was performed. In the remaining cases, cesarean section was performed for reasons other than the myomas.

Comment

Bonney, in 1918⁴ and in 1922,⁵ and W. J. Mayo^{6, 7} and other authors advised myomectomy, if feasible, instead of hysterectomy in the treatment of uterine myomas in cases in which the patients are women of the childbearing age. To substantiate their statements they reported a significant number of cases in which good results were obtained. In cases of uterine fibromyoma in which the patients are young women, operative treatment commonly is undertaken because of excessive bleeding and an operation sufficiently complete to control this symptom must be performed. It is evident that in many cases the final selection of the type of operation cannot be made until the abdomen has been opened. In some cases hysterectomy is necessary. Consequently, before the operation is undertaken, the patient should be informed that the final decision relative to conservation of the reproductive function cannot always be made preoperatively.

Our experience, as well as that of other authors, indicates that myomectomy has very little effect on the course of future pregnancies. In our series of cases the incidence of complications of delivery increased somewhat, but with modern obstetric and surgical care the increased risk certainly is not prohibitive. As previously stated, in 101 of the 250 cases, pregnancy occurred 167 times after myomectomy was performed. In 135 of the 167 instances the pregnancy continued to term or nearly to term. In twelve, or 9 per cent, of the 135 instances the child was delivered by cesarean section. It is evident, therefore, that cesarean section was required more frequently than it is in an average group of obstetric cases.

It is difficult to evaluate the role of uterine myomas as a cause of infertility without the benefit of a complete examination of all factors influencing fertility in both men and women. It frequently is not possible to investigate safely tubal patency in the presence of myomas which are producing symptoms. The opinion prevails that the fertility of women decreases in the presence of myomas. The fact that only eight of eighty-two patients who complained of infertility prior to myomectomy subsequently conceived would seem to be in agreement with this statement, although we have no knowledge of other factors which may have contributed to the infertility. It is significant, how-

ever, that Brewer and Jones⁸ did not find evidence of abnormal physiologic activity of the ovaries in their studies of the corpus luteum and endometrium in cases of uterine myoma.

The term "recurrence" has been applied to the subsequent appearance of uterine myomas after myomectomy. Bonney^{9, 10} has emphasized repeatedly the incorrectness of this term. Perhaps the term "reappearance" is better than "recurrence." Bonney has said that "recurrences" represent the growth of small myomas that were actually present at the time of myomectomy or the development of entirely new growths. He said that fibroids reappeared in only nine of 379 cases. The explanation of this amazingly low figure is probably due to Bonney's performance of a most complete myomectomy. Frequently, in the course of operation, he opened the uterine cavity to avoid overlooking a tumor. He emphasized the advisability of removing all myomas and illustrated his opinion by stating that in one case he removed 125 separate tumors. Significant uterine myomas appeared subsequent to myomectomy in 30 per cent of our 250 cases. Further treatment was required in 20 per cent of the 250 cases. The chance that further treatment may be necessary will have to be assumed by the patient in exchange for the attempt to preserve the function of reproduction. It is interesting to note that those patients who did not become pregnant after myomectomy showed a slightly higher incidence of "recurrence" than did those who subsequently became pregnant.

A brief résumé of the cases in which myomectomy was performed in the course of pregnancy has been given in order to emphasize two points. First, in the course of pregnancy complicated by uterine myomas, conditions may arise which require surgical treatment. Second, myomectomy does not carry undue risk for the pregnant women but the fetal mortality is high; in twenty-three cases of intrauterine pregnancy in this series, only ten infants survived. Because of relatively high fetal mortality, removal of myomas from the pregnant uterus should be done only in cases in which the indications are compelling.

A salvage of 128 children in 167 instances of pregnancy in 101 women, who previously had undergone uterine myomectomy instead of hysterectomy or irradiation for fibroids, seems to justify myomectomy in selected cases in which the patients are women of the child-bearing age. It is recognized that after myomectomy, patients run more risk of remote postoperative complications, such as intestinal obstruction, than they do after hysterectomy, which can be accompanied by peritonealization.

REFERENCES

1. Mussey, R. D., and Hardwick, R. S.: AM. J. OBST. & GYNEC. 29: 192, 1935.
2. Pierson, R. N.: AM. J. OBST. & GYNEC. 14: 333, 1927.
3. Counsellor, V. S., and Bedard, R. E.: J. A. M. A. 111: 675, 1938.

4. Bonney, Victor: Brit. M. J. 1: 278, 1918.
5. Bonney, Victor: J. Obst. & Gynaec. Brit. Emp. 29: 591, 1922.
6. Mayo, W. J.: J. A. M. A. 74: 1685, 1920.
7. Mayo, W. J.: Surg., Gynec. & Obst. 34: 548, 1922.
8. Brewer, J. I., and Jones, H. O.: AM. J. OBST. & GYNEC. 41: 733, 1941.
9. Bonney, Victor: Lancet 1: 171, 1931.
10. Bonney, Victor: J. Obst. & Gynaec. Brit. Emp. 44: 1, 1937.

Discussion

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—When fibromyomas of the uterus cause symptoms which necessitate surgical intervention for their relief, the age of the patient must influence the surgical procedure performed. In many cases it is necessary to preserve the menstrual function because of the psychic depression which is produced in a young woman by the loss of her menses and her child-bearing availability. Myomectomy for the relief of sterility should only be considered if the lesion is an obstruction to the ovum or is responsible for menstrual disturbances and the resultant endometrial changes, and after all other studies have failed to reveal the cause of the infertility. Great care must be exercised in those patients presenting themselves because of increased bleeding, as this may be an endocrine imbalance in which the associated myoma plays no part. Unless the myoma disturbs the endometrium because of its close proximity or direct interference, it most likely is not responsible for the menstrual disturbance.

That pregnancy will follow myomectomy is shown by the statistics of the authors. If we were given more data about previous fertility studies in these eight cases and the associated pathology found at the time of operation, other causes responsible for the infertility might be revealed. We should hesitate to advise myomectomy for the relief of sterility if other indications for surgical therapy do not exist. Campbell, in his report of a series of cases from the Johns Hopkins Clinic, has shown that pregnancy may exist in a myomatous uterus with little serious disturbance during pregnancy or the first stage of labor. The incidence of forceps delivery was higher in the second stage and in the third stage, postpartum hemorrhage and adherent and retained placenta were found to occur more frequently. During the puerperium involution was often delayed.

Myomectomy during pregnancy should be reserved for those cases showing definite symptoms of degeneration of the tumor because of interference or disruption of blood supply. Pain or tenderness over a tumor without other signs of degeneration or the finding of a tumor should not be considered as cause for surgical interference. If the tumor is obstructive because of its location in the pelvis, the patient should be carried to term and then have the tumor removed at the time of section.

The slightly higher incidence of complications occurring with pregnancy following myomectomy should not influence our choice of the procedure. As stated by the authors, "With modern obstetric and surgical care the increased risk certainly is not prohibitive."

DR. EMIL NOVAK, BALTIMORE, MD.—It is quite generally agreed that in some as yet unknown fashion myomas of the uterus tend to produce at least a relative infertility. On this point my viewpoint is different from that of Dr. Schmitz, because I believe that myomectomy is not infrequently indicated in the case of young women who are extremely anxious for children and in whom careful study has apparently eliminated other causes of sterility. Anyone who has carried out this procedure in any great number of cases must have been impressed with the considerable proportion of successes which it yields, pregnancy often occurring rather promptly after operation following even years of sterility. Certainly the justification for myomectomy even with tumors which are symptomless except for

the associated sterility is far greater than, for example, the performance of tubal plastic procedures in sterility due to tubal closure. Even these are justified if, but only if, the patient understands fully the slimness of her chances.

A further advantage of myomectomy for this indication is that these tumors undoubtedly in some cases predispose to miscarriage in the event of pregnancy. Finally, if myomectomy is not done, the tumors may later show such increase in size and number that hysterectomy rather than myomectomy may be considered necessary, and the patient's chances for children are forever lost.

While in most myomectomies we deal chiefly with intramural or subperitoneal growths, we should not hesitate to invade the uterine cavity should this be necessary. In one of my patients a vaginal hysterotomy was done for a rather large submucous growth, but the operation revealed numerous other growths, submucous or interstitial, which could be peeled out from within the uterus. It seemed that practically all the endometrium was removed, and yet this woman became pregnant within a few months and was later safely delivered by cesarean section.

DR. JAMES E. DAVIS, ANN ARBOR, MICH.—The position of the myoma may determine the safety of its removal. Some subserous myomas can be removed as easily as warts from the skin surface. The blood supply of the tumor may also determine the safety of its removal. Finally, the histologic structure may have an important bearing upon the safety. A myoma that is degenerating may be quite safe to remove, while one that has a rich blood supply, is composed of rich muscle structure, and is in a position to interfere with the continued normal physiology of the uterus cannot be removed very easily nor with much safety.

RUPTURE OF THE UTERUS*

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RUPTURE of the uterus has occurred at the Boston City Hospital forty-four times in the last twenty-five years. During this period there have been 41,706 deliveries, which is an incidence of 1 in 1,118. In considering the occurrence of rupture of the uterus in a clinic conducting an emergency service, it must be realized that the frequency of this condition is high because of the number of complicated and poorly handled cases which are referred to the hospital after the patients have been in labor for many hours. It also may be stated that the incidence of ruptured uteri occurring at home is probably greater than the actual number of cases which are reported. This is due to the fact that many have produced little in the way of symptoms to arouse concern or are wrongly diagnosed. Some are purposely overlooked, such as the fatal cases which occur following accouchement forcé or the injudicious use of pituitrin. The deaths in these cases not infrequently are reported as being due to hemorrhage and shock.

Causes

The causes of rupture may be classified as traumatic and nontraumatic. In the first group are included those cases which are associated with external trauma, such as a fall or blow, internal podalic version, accouchement forcé, the use of forceps through an incompletely dilated cervix, and the manual removal of the placenta. Additional external trauma may have its origin in the unskillful introduction of forceps blades, the forceful rotation of the posterior fetal head, or the manipulation of destructive instruments for the removal of a dead fetus.

Forceps failure followed by version constituted the most frequent cause of ruptured uterus in the traumatic group in this series of cases. This sequence of events must be considered as having been due to an error in obstetric judgment. If the head after many hours of labor cannot be pulled through the pelvic brim, it is incontrovertible evidence that the patient should have been delivered by cesarean section, and in many cases this operation could have been done after the patient had a reasonable test of labor.

The reprehensible dragging of a head with traction forceps through an undilated cervix is an obvious cause of rupture of the uterus. The

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TABLE I. CLASSIFICATION OF CASES ACCORDING TO CAUSE

NUM- BER OF CASES	TYPE OF CASE	PER- CENT- AGE OF TOTAL NUMBER	MOTH- ERS DEAD	MOTH- ERS LIVING	MATER- NAL MOR- TALITY (PER CENT)	BABIES DEAD	BABIES LIVING	FETAL MOR- TALITY (PER CENT)
12	Forceps failure and version	27	8	4	66	9	3	75
11	Previous cesarean section	25	5	6	45	10	1	90
8	Version, trans- verse presenta- tion	18	5	3	62	8	0	100
5	Spontaneous rup- ture	11	0	5	00	5	0	100
1	Manual removal of placenta	2	1	0	100	1	0	100
1	High forceps	2	0	1	00	1	0	100
1	Low forceps, im- pacted shoulders	2	0	1	00	1	0	100
1	External trauma	2	1	0	100	1	0	100
1	Normal delivery	2	1	0	100	0	1	00
1	Pituitrin	2	1	0	100	1	0	100
1	Accouchement forcé	2	0	1	00	1	0	100
1	Hydrocephalus, version	2	1	0	100	1	0	100
44			23	21	52	39	5	89

use of instruments, even in cases in which the cervix is thought to be fully dilated, can occasionally result in marked damage because, until the head is on the perineum and in sight, complete retraction of the cervical os has not taken place.

If the lower uterine segment has thinned out to its greatest capacity, it is understandable that cervical dilatation, which would ordinarily result in a simple tear, might cause the splitting of the overstretched lower uterine segment. The application of forceps in the high or mid-position, particularly if a slight rim of cervix is present, results in a forceful dilatation which may produce a tear involving the lower uterine segment. Rarely does a tear which accompanies a normal delivery extend beyond the cervix, but this unfortunate accident occurred in one of our cases, resulting in the patient's death.

The absence of placenta previa from this series of cases may be explained by the reason that very few patients at the Boston City Hospital with this diagnosis have been delivered other than by cesarean section in the past twenty-five years. This condition was formerly responsible for many cases of ruptured uterus, particularly so when the treatment adopted was the indefensible accouchement forcé. As a result of the placenta being inserted in the lower uterine segment in these cases, this part of the uterus is extremely soft and friable and any attempts at artificial dilatation frequently result in extensive tearing. This is also true even when hydrostatic bags are used. After the expulsion of the largest bag, cervical dilatation remains incomplete, and when

the head is drawn through the cervix with the use of forceps or version, a tear occurs which frequently involves the lower uterine segment with the production of a ruptured uterus.

The nontraumatic causes for rupture of uterus may be listed as scars in the uterine wall due to previous cesarean section, curettage, salpingectomy with removal of uterine cornu, the manual removal of an adherent placenta, fatty or fibrous degeneration of the uterine musculature, faulty development and malposition of the uterus, multiparity, and multiple pregnancy. Additional contributing causes may be malignancy, hydramnios, abruptio placentae, and inflammation associated with previous puerperal sepsis. To these may be added dystocia due to a contracted pelvis, a postmature or excessively large fetus, hydrocephalus, or shoulder or other malpresentation. Interstitial pregnancy or pregnancy occurring in one of the horns of a bicornate uterus may be further etiologic factors.

The use of oxytocic drugs before the completion of the first stage of labor is unquestionably an important cause of rupture of the uterus. It is interesting to note that in this series of cases only once did the history disclose that pituitrin had been used in the first stage. Naturally, the practitioner is very reluctant to volunteer the information or dares not admit that the disaster is due to his ill-advised administration of this drug.

There have been a small number of cases reported where rupture has occurred during pregnancy or at the commencement of labor and where no causative factor could be found—no developmental abnormality, no uterine scar, no accompanying trauma, and no previous uterine manipulation. Histologic examination contributes nothing to account for the accident. I have seen in another hospital a spontaneous rupture of the uterus in an early pregnancy which the pathologist reported as being due to an overactive nidation of the ovum with excessive autolysis of the maternal tissues from the trophoblastic elements. This succession of events may be an etiologic factor in some of those obscure cases.

Repeat Cesarean Section

Of the nontraumatic factors, the one which contributes by far the greatest number is the rupture occurring following a previous cesarean section. In this group the number of cases was eleven, amounting to 25 per cent of the total. Although ruptured uterus from this cause forms one of the largest groups in any series of cases, the mortality is less than for the other varieties. The reason for this is the comparative avascularity of the scar which reduces the amount of hemorrhage and the lessened incidence of infection because vaginal examination is unnecessary and operative deliveries have not been made or at-

TABLE II. REPEAT CESAREAN CASES

METHOD OF TREATMENT	NUM- BER OF CASES	MOTH- ERS DEAD	MOTH- ERS LIVING	MATER- NAL MOR- TALITY (PER CENT)	BABIES DEAD	BABIES LIVING	FETAL MOR- TALITY (PER CENT)
Hysterectomy	4	1	3	25	4	0	100
Resuture	5	2	3	40	4	1	80
Condition too poor for operation	2	2	0	100	2	0	100

tempted. This accident may occur during labor as a result of uterine contractions or it may take place in the last several weeks of pregnancy before labor begins.

A defective scar may be caused by the imperfect approximation of the uterine wound due to retraction of the muscle fibers after incision or by stitches placed too far apart. The use of very tight sutures may produce pressure necrosis and gaping defects or sloughing; also, the occurrence of a hematoma or the inclusion of the serous coat in the repair of the uterine wound may be causes of faulty healing.

The element of sepsis is also an important obstacle to satisfactory healing. The ideal result in the uterine wound is a complete regeneration of the muscular tissue, and although this desirable result can and does occur, the healing of smooth muscle wounds in general is accomplished by scar tissue formation.

D'Acerno states that of the very considerable amount of investigation that has been made of classical cesarean wounds, only nine deal with intact scars. Greenhill and Bloom, in a study of uterine scars in thirty-seven cases, found healing by scar tissue in thirty-one, or 84 per cent. Schwarz and Paddock, in their very complete work on the histology of the cesarean scar, conclude that muscle regeneration plays a very minor part in the healing and consider fibroblastic proliferation as practically normal healing.

But, although the uterine scar is satisfactory and competent, there is at present no means known of determining this very important fact, and even though sepsis and imperfect wound closure are causes of a faulty scar, it is also true that rupture can occur following an entirely normal convalescence and perfect surgical technique.

The insertion of the placenta over the scar in a subsequent pregnancy is thought to be a contributing element in producing these weakened wounds. Some authorities insist, however, that if the wound has healed without interference, the development of the placenta in this location should be of no consequence. Their contention is that it is the granulation tissue which is present, as a result of second intention healing, which is invaded by the chorionic elements, thus producing the imperfect scar.

It is an established fact that the classical type of cesarean section is responsible for a much larger number of ruptured uteri than the low cervical operation. In an article comparing these two operations, Phaneuf reports 25 per cent of rupture following the classical operation as against 3 per cent following the low cervical operation. Also, in a report published by Bloom and Greenhill of ruptures occurring after the low operation, the accident happened only in patients who had been in labor for considerable time and none took place during pregnancy.

An important reason for rupture occurring less frequently in the low cervical operation is that the incision is made in the nonmotile part of the uterus. In the classical operation with the wound in the fundus, the suture line is continually shaken up by the contraction and relaxation of the uterus during the puerperium, producing a condition which militates against healing. Since overdistention of the scar and invasion of it by the embryonal elements of the placenta are considered as contributing causes to a weakened scar, clearly the cicatrix is less apt to be affected by these factors in the low operation than in the fundal variety.

It is important, however, to realize that the low operation has only comparatively recently been universally employed, and although the incidence of rupture following it has been markedly reduced, it does occur, and with the passage of time the reports following this accident will undoubtedly increase.

Formerly, it very definitely was felt that any patient who had had a cesarean section should have all subsequent pregnancies terminated in the same manner. In the last several years this idea has undergone considerable modification, and there has been a definite swing away from the dictum "once a cesarean, always a cesarean." Of course, if the original indication is still existent, such as contracted pelvis, a cesarean would naturally have to be done with each pregnancy. If, however, a multiparous patient has had the operation for some intercurrent indication such as a placenta previa or a separated placenta, it has been thought that she might be permitted to have a trial labor in a subsequent pregnancy and, if no untoward symptoms arose, to continue and be delivered from below. The success or failure of such a procedure obviously depends on the competence of the scar in the uterus. As stated, however, there is unfortunately no criterion upon which this decision can be made. It is advisable in the conduct of these cases to consider any departure from normal, or the appearance of the slightest untoward symptoms, as being those of rupture or beginning rupture and to open the abdomen immediately.

It should also be realized that even though the patient has been successfully delivered from below following a cesarean section, a rupture can occur in subsequent pregnancies. In a case reported by

Lazard, the patient had gone through two rapidly succeeding pregnancies following a cesarean section. These labors were long and hard and were without incident. She ruptured the uterus in the next pregnancy before the onset of labor.

Types of Rupture

Two types of rupture of the uterus are recognized: the complete and the incomplete variety. In the former, the mucosa, the muscular uterine wall, and peritoneal covering are torn through and there is a communication with the peritoneal cavity, while in the latter only the uterine mucosa and muscle are involved, the peritoneal covering of the uterus remaining intact.

In the complete variety the baby and placenta are frequently found in the peritoneal cavity, and the contracted, inactive uterus is felt low in the pelvis beside it. Occasionally the vertex is securely wedged in the pelvis and the rest of the fetus has escaped through the uterine rent.

The complete variety occurs more frequently than the incomplete. In this series there were twenty-five complete ruptures and nineteen of the incomplete type. In a group of cases Lobenstein found forty-six of the complete and twenty-nine of the incomplete, and Merz counted one hundred eighteen complete and forty-six incomplete ruptures in his series.

In the incomplete type the rupture extends frequently into the part of the uterus found between the leaves of the broad ligament, on either side. The reason for this is that during pregnancy the folds of the peritoneum draping the broad ligaments are loose and somewhat separated as a result of the general hypertrophy and enlargement of the uterus during pregnancy. In the incomplete ruptures the baby usually remains in the uterus but may only be separated from the peritoneal cavity by the uterine serosa.

Diagnosis

The signs and symptoms of rupture are usually discernible but in occasional cases may develop so gradually as to escape detection. In the course of a tedious labor the contractions may become irregular and the uterus may fail to relax completely in the interval between the pains. There may be prominence and tension of the round ligaments accompanied by a development and a rising up of the contraction ring. There may be little or no interval between the uterine contractions or the uterus may be tender to palpation between the pains. The pulse rate increases and may become irregular.

When the actual rupture takes place, the signs of hemorrhage and shock usually are manifest. It should be pointed out, however, that the presence of external bleeding is not constant and, therefore, its

TABLE III. CASES TREATED BY LAPAROTOMY—EXCLUSIVE OF REPEAT CESAREAN CASES

METHOD OF TREATMENT	NUM- BER OF CASES	MOTH- ERS DEAD	MOTH- ERS LIVING	MATER- NAL MOR- TALITY (PER CENT)	BABIES DEAD	BABIES LIVING	FETAL MOR- TALITY (PER CENT)
Complete hysterectomy	4	2	2	50	3	1	75
Supravaginal hysterectomy	18	6	12	33½	16	2	89
Resuture	3	1	2	33½	1	2	33½

absence should have no diagnostic import. If, on the other hand, bleeding suddenly appears in the course of labor, particularly in a difficult or abnormal labor, it should be considered as extremely suggestive of the beginning of a tear in the lower uterine segment and a thorough examination should be made with this possibility in mind. The appearance of shock accompanying a cessation of labor and a recession of the presenting part are particularly ominous symptoms. The patient who has been in intense pain as a result of hard labor may at once seem temporarily greatly relieved. The fetal heart almost always shows evidence of distress by an aberration in its regularity and rate.

In the more violent type of case the labor may be tumultuous and during the acme of a uterine contraction, accompanying a particularly severe pain, the patient may have the feeling that something has given away in her lower abdomen. In the completely ruptured uterus in which the fetus escapes into the abdominal cavity, the baby may be felt with startling clearness immediately beneath the examining fingers and the contracted uterus as a firm globular mass beside it. The signs of shock and hemorrhage quickly appear.

The partial rupture may, on the other hand, produce symptoms which are comparatively very slight. This is especially true if the rupture occurs in the region of one or the other of the broad ligaments and the hemorrhage results in a hematoma between its leaves. The signs of collapse and hemorrhage may not be present until a secondary rupture takes place into the abdominal cavity or counterpressure is removed by the extraction of the fetus, permitting an exacerbation of the bleeding.

If the uterine rupture occurs following an obstetric procedure from below, with the cervix not properly and completely dilated, there may be profuse vaginal bleeding immediately following the extraction of the baby.

It sometimes happens that in spite of proper preparation of the cervix, a tear may occur which involves the lower uterine segment but which may not be extensive enough to cause marked bleeding or accompanying shock. This patient will complain of persistent, severe, low abdominal pain following delivery, and usually a vaginal exami-

nation with exploration of the lower uterine segment will establish the diagnosis.

In many obstetric clinics it is a rule after all versions, breech extractions, and difficult instrumental deliveries to make a routine examination and inspection of the cervix and lower uterine segment. If an extensive tear or rupture is found, appropriate treatment is instituted at once.

TABLE IV. CASES REPAIRED FROM BELOW AND WITH INTRAUTERINE AND VAGINAL PACK

	NUMBER	LIVING	DEAD	MORTALITY (PER CENT)
Mothers	7	1	6	86
Babies	7	2	5	71

TABLE V. MORTALITY RATE FOR ENTIRE SERIES

	NUMBER	LIVING	DEAD	MORTALITY (PER CENT)
Mothers	44	21	23	52
Babies	44	5	39	89

Prognosis

The maternal mortality in this series of cases was 52 per cent and the fetal mortality, 89 per cent. The prognosis for the baby is invariably bad, due to the interference with the placenta which is usually wholly or partially detached. The most important factor in the outcome for the mother is the promptness with which the diagnosis is made and with which appropriate treatment is instituted. The invaluable and irretrievable time that is frequently lost here, with the accompaniment of hemorrhage and shock and later sepsis, is the powerful factor which results too frequently in a fatal termination.

One of the important features influencing the outcome is whether the placental site has been involved and if a large blood vessel has been injured. These circumstances obviously affect the amount of hemorrhage caused, and they also are an influencing element in the amount of sepsis which follows.

Maternal death from bleeding, when it happens, usually takes place almost immediately following the uterine rupture. Occasionally it may be delayed from twenty-four to forty-eight hours, especially in the cases in which the bleeding has taken place into the space between the leaves of the broad ligaments. Here, not infrequently, when the baby is delivered either abdominally or vaginally, the bleeding recurs because the fetus has been acting as a plug or tampon.

It must also be realized that if the patient survives the initial danger of shock and hemorrhage, there remains lurking in the background the very considerable element of sepsis.

Treatment

An important method of dealing with the problem of ruptured uterus is the prevention of its occurrence. It frequently is the result of unintelligent expectancy on the part of the attendant, and for this reason the condition rarely occurs in properly conducted and well-supervised hospitals. The majority of the cases occur in the home and in women whose labors have been poorly managed.

If any condition exists which may result in dystocia, the possibility of ruptured uterus should be kept in mind. Transverse presentation should be watched particularly, and delay in cervical dilatation, if present, should be aided by the use of a bag and the patient should be promptly delivered by version as soon as the cervix is fully dilated. The primipara starting in labor with an unengaged head and the multipara with unengagement after one hour of satisfactory second-stage pains should be considered as candidates for this condition. If the presence of a contraction ring becomes apparent, the labor should be immediately terminated by appropriate measures—with forceps if the cervix is fully dilated and no cephalopelvic disproportion exists, by cesarean if necessary, and never by version.

The treatment of choice in a case of ruptured uterus is an abdominal operation immediately after the rupture has occurred, with a supravaginal or complete hysterectomy. The decision as to whether a supravaginal or a complete hysterectomy is done should be influenced by whether the cervix has or has not been involved and the probable amount of sepsis present. If rupture has occurred and the baby is still in the uterus, it is important that it be not extracted from below because of the practical certainty of extending the rupture, aggravating the bleeding, and contributing further to the shock.

Rarely, if the rupture takes place in the first pregnancy with the loss of the baby and the patient is extremely desirous of having a child, the tear in the uterus may be sutured and the organ retained. This, however, should be restricted to uteri in which the torn edges are not too irregular or too badly traumatized and where the question of sepsis is not too prominent. All women in whom a ruptured uterus has been repaired should, of course, have a subsequent pregnancy terminated by a cesarean section.

If the patient is one who has had a previous cesarean section, the rupture invariably takes place in the uterine scar. If the placenta has been inserted in this location, the bleeding may be excessive and the best results are probably obtained by hysterectomy. If the scar is not the site of the placental implantation, usually there is comparatively little bleeding from the scar tissue which forms the edges of the torn surface, and it may be possible to freshen these surfaces and resuture the wound. The actual results from the point of view of mortality in these two methods of treatment following a previous cesarean sec-

tion are about the same. The resuture method preserves the uterus for possible future pregnancy and, it should be added, for a possible future rupture.

If the condition of the patient is poor, and it is felt that she cannot stand a hysterectomy, a resuture may perhaps be more quickly done, with the intention of possibly removing the uterus later if it seems necessary.

In the type of uterine rupture which takes place in the women who have been delivered from below, a cervical tear has invariably occurred, which, by extension, has involved the lower uterine segment. The rupture may have been found in the routine vaginal examination following an instrumental delivery or version, or sharp bleeding occurring in the second stage of labor may have directed attention to its presence. If not too extensive, this type of tear may, in some cases, be reached and taken care of vaginally, the upper angle of the wound being exposed and repaired by a series of traction sutures applied one above the other. In addition to this, pressure and counterpressure are secured by means of a firm intrauterine and vaginal pack.

It may be stated in general that in the delivered woman with hemorrhage from deep cervical lacerations, the attempt to control the condition with a uterine pack, vaginal tamponade, and firm abdominal and T binders, plus the use of ice and ergot, has a very small place in modern obstetric clinics. It may, however, be of occasional value to the practitioner who has the misfortune to encounter this condition amid unfavorable surroundings and who is without available hospital facilities.

In neglected cases, with dead babies, destructive operations may be the least evil way to handle the difficulty. If the head, in the case of hydrocephalus, is the presenting part, it may be drained through the cervix by means of a spinal puncture needle, drawing off sufficient fluid to permit the delivery, even with living babies. This procedure is not at variance with ecclesiastic views.

The mortality from hemorrhage and shock in the last few years has been very remarkably influenced by the simplified methods of obtaining and giving blood. The general availability of dry plasma and the increasing establishment of hospital blood banks with the frequent use of frozen plasma and refrigerated blood have notably diminished one of the major causes of death in these cases.

Conclusions

1. At the Boston City Hospital in the last twenty-five years and in 41,706 consecutive cases, rupture of the uterus occurred forty-four times, an incidence of one in 1,118 cases. The maternal mortality in this series of cases was 52 per cent and the fetal mortality 89 per cent.

2. This figure is no accurate index of the percentage of the occurrence of ruptured uterus as that number will vary with the size of the

area served by the emergency service. Also, many cases are unreported, due to inaccurate diagnosis, deliberate or otherwise.

3. The prognosis is very definitely influenced by the amount of time which elapses between the occurrence of the rupture and the establishment of proper treatment.

4. Most of the cases are preventable as they occur chiefly in women in whom ill-advised obstetric procedures have been undertaken to hasten the delivery of the baby or in patients who have been given oxytocic drugs.

5. The rupture of the uterus during pregnancy or labor following a cesarean section occurs frequently. Here, the prognosis for the mother is far better than in other cases of complete rupture.

6. It is extremely hazardous to permit a woman who has had a cesarean section for a nonpelvic indication to be delivered subsequently from below.

7. Women who have had a previous cesarean section should have the strictest supervision and attention in the last weeks of pregnancy, and if another section is decided upon, it should be done a week or ten days in advance of the expected date.

8. The treatment which has produced the best results is laparotomy and either supravaginal or complete hysterectomy. In occasional cases it may be permissible to repair the rupture in an attempt to conserve the uterus for a possible subsequent pregnancy.

9. Palliative measures may be considered only in the lesser degrees of incomplete rupture or where hospital facilities are not available.

10. The universal availability of dried plasma and the general prevalence of blood banks should definitely reduce the mortality of this condition.

11. Any discussion of ruptured uterus can properly include the ob-
jurgation of Milne Murray, who states, "It may, I think, be safely said that the occurrence of a case of rupture of the uterus in the hands of an obstetrician is, in the great majority of cases, a reproach to him and a slight to his art."

References

- Audebert, J. L.: *La cicatrice utérine après la section césarienne*, *Gynéc. et Obst.* 7: 487-500, 1923.
- Bell, John Norval: *Rupture of the Uterus in Cesareanized Women, With a Review of the Literature on This Subject to Date*, *Am. J. Obst.* 74: 950-954, 1916.
- Bell, Rudolph: *Rupture of the Uterus During Labor*, *J. M. A. Georgia* 22: 342-344, 1933.
- Bey, Naguib Mahfouz: *Rupture of the Uterus*, *J. Obst. & Gynaec. Brit. Emp.* 39: 743-758, 1932.
- Blevins, W. J.: *Rupture of the Uterus. Report of Cases*, *California & West. Med.* 32: 111-113, 1930.
- Breitstein, Louis I.: *Rupture of the Uterus Following Cesarean Section With a Study of the Uterine Scar*, *J. A. M. A.* 62: 689-691, 1914.
- Burkons, H. F.: *Ruptured Uterus*, *AM. J. OBST. & GYNEC.* 42: 75-81, 1941.

- D'Acierno, P.: Spontaneous Rupture of the Uterus in Pregnancy Following a Previous Classic Cesarean Section, *Am. J. Surg.* 19: 315-320, 1933.
- Davies, D. J.: Rupture of Uterus, *Ohio State M. J.* 33: 1101-1104, 1937.
- Davis, A. B.: Ruptured Uterus, *AM. J. OBST. & GYNEC.* 13: 522-528, 1927.
- DeLee, Joseph B.: The Use of Solution of Posterior Pituitary in Modern Obstetrics, *J. A. M. A.* 115: 1320-1326, 1940.
- Delmas, P.: Vingt ans de pratique des rachi en obstétrique, *Liège méd.* 32: 877-880, 1939.
- Delmas, Paul: Some Concluding Remarks Concerning the Elective Evacuation of the Uterus at the End of Pregnancy, *J. Obst. & Gynaec. Brit. Emp.* 38: 97-102, 1931.
- DeSa, H. D.: Spontaneous Intrapartum Rupture of the Uterus in a Case of Placenta Praevia, *J. Obst. & Gynaec. Brit. Emp.* 41: 963-967, 1934.
- Eden, Thomas Watts: The Operative Treatment of Rupture of the Uterus, With an Account of Three Cases Treated by Abdominal Hysterectomy, *J. Obst. & Gynaec. Brit. Emp.* 15: 363-381, 1909.
- Fothergill, W. E.: Three Cases of Injury of the Parturient Canal, *J. Obst. & Gynaec. Brit. Emp.* 8: 403-407, 1905.
- Gelle, P.: Grossesse gémellaire; éclamptie; césarienne basse, *Bull. Soc. d'obst. et de gynéc.* 21: 62-63, 1932.
- Gerrard, E. A.: A Case of Rupture of the Uterus, *Lancet* 1: 182, 1929.
- Greenhill, J. P., and Bloom, Benson: Histologic Study of Uterine Scars After Cervical Cesarean Section, *J. A. M. A.* 92: 21-26, 1929.
- Grimsdale, T. B.: Rupture of the Uterus During Labor. Abdominal Hysterectomy, *J. Obst. & Gynaec. Brit. Emp.* 4: 558-561, 1903.
- Healy, T. M.: Notes on Five Cases of Rupture of the Uterus During Labor, *J. Obst. & Gynaec. Brit. Emp.* 37: 827-831, 1930.
- Hoffman, W. E.: Ruptured Uterus, *West Virginia M. J.* 35: 74-76, 1939.
- Holland, Eardley: Discussion on Rupture of the Cesarean Section Scar in Subsequent Pregnancy or Labor, *Proc. Roy. Soc. Med. (Sect. Obst. & Gynaec.)* 14: 22-124, 1920.
- Holland, Eardley: Rupture of the Cesarean Section Scar in Subsequent Pregnancy or Labor, *J. Obst. & Gynaec. Brit. Emp.* 28: 488-522, 1921.
- Ivanoff, N.: Del'etiologie, de la prophylaxie et due traitement des ruptures de l'uterus pendant l'accouchement, *Ann. de gynec. et d'obst.* 1: 449-465, 1904.
- Kerr, J. Munro, and Hendry, James: Uterine Scars (Report of Section of Obstetrics and Gynaecology, Royal Society of Medicine, June 5, 1924), *Brit. M. J.* 1: 1093-1094, 1924.
- Knowles, Joseph J.: Rupture of the Uterus, *M. Rec.* 144: 125-129, 1936.
- Lawson, A. F., and Gordon, T. B.: Rupture of Uterus During First State of Labor, *West Virginia M. J.* 27: 559-560, 1931.
- Lazard, E. M.: Report of a Case of Ruptured Uterus Through a Cesarean Scar, *California State J. Med.* 17: 109-110, 1919.
- Long, Jerome P., Jr.: Uterine Rupture Involving the Vagina and Bladder With Recovery, *South. M. J.* 30: 1028-1030, 1937.
- Losee, J. R.: The Cesarean Scar, an Anatomical Study, *Am. J. Obst.* 76: 1-14, 1917.
- Lynch, Frederick J.: Rupture of the Uterus, *New England J. Med.* 221: 847-850, 1939.
- McNeile, Lyle G., and McBurney, Raymond D.: Statistical Study of Uterine Ruptures, *California & West. Med.* 42: 73-79, 1935.
- McPherson, Ross: Multiple Cesarean Section, With the Results in Thirty-Nine Cases Done at the New York Lying-In Hospital, *Bull. Lying-In Hosp., City of New York* 7: 181-188, 1911.
- Mason, Nathaniel R., and Williams, John T.: The Strength of the Uterine Scar After Cesarean Section. An Experimental and Clinical Study, *Boston M. & S. J.* 162: 65-72, 1910.
- Murray, R. Milne: A Case of Spontaneous Rupture of an Apparently Normal Uterus at the Commencement of Labor, *J. Obst. & Gynaec. Brit. Emp.* 1: 142-151, 1902.
- Novak, Emil: Rupture of the Uterus Through the Cesarean Section Scar, *J. A. M. A.* 71: 105-106, 1918.
- O'Connor, Cornelius T., and Gorman, Arthur J.: The Treatment of Hydrocephalus in Cephalic Presentation, *AM. J. OBST. & GYNEC.* 43: 521-524, 1942.
- Phaneuf, L. E.: Obstetric Future of Women Delivered by Low or Cervical Cesarean Section, *AM. J. OBST. & GYNEC.* 13: 446-457, 1927.

- Racker, D. C.: Spontaneous Rupture of the Uterus, *AM. J. OBST. & GYNEC.* 67: 242-248, 1938.
- Reese, J. Morris: Ruptured Uterus, *West Virginia M. J.* 37: 402-406, 1941.
- Richards, C. E. B.: Uterine Rupture Following Cesarean Section, *Brit. M. J.* 1: 1359-1361, 1938.
- Riddel, James: Rupture of the Uterus During Pregnancy, *J. Obst. & Gynaec. Brit. Emp.* 33: 1-16, 1926.
- Rongy, A. J.: Rupture of the Cesarean Scar, *Am. J. Obst.* 74: 954-967, 1916.
- Roxas, B., Baens, A., and Katigbak, J. R.: Rupture of the Uterus: Report of Cases in the Philippine General Hospital From 1910 to November, 1933, *J. Philippine Islands M. A.* 14: 37-41, 1934.
- Schwartz, Leo S., and Kurzrok, Lawrence: Spontaneous Rupture of the Uterus, *AM. J. OBST. & GYNEC.* 31: 1038-1041, 1936.
- Schwarz, Otto H., and Paddock, Richard: The Cesarean Scar, *AM. J. OBST. & GYNEC.* 10: 153-171, 1925.
- Seley, Abbey David: An Analysis of Twelve Cases of Spontaneous Rupture of the Pregnant Uterus, *AM. J. OBST. & GYNEC.* 33: 857-863, 1937.
- Sheldon, Charles P.: A Record of Twenty-Six Cases of Rupture of the Uterus, *AM. J. OBST. & GYNEC.* 31: 455-466, 1936.
- Skeel, A. J., and Jordan, F. F.: A Consideration of Cesarean Section, With a Survey of 1,047 Cases in the Cleveland Registration Area in Five Years, *AM. J. OBST. & GYNEC.* 23: 172-187, 1932.
- Slevin, John George: Spontaneous Rupture of the Uterus Following a Previous Cesarean Section. Case Report and Discussion, *J. Michigan M. Soc.* 37: 506-509, 1938.
- Smith, A. Lionel: A Series of Ten Cases of Complete Rupture of the Uterus, *J. Obst. & Gynaec. Brit. Emp.* 15: 382-395, 1909.
- Stapleton, Grace: Rupture of Uterus Early in the First Stage of Labor, *Brit. M. J.* 1: 893-894, 1928.
- Weber, George H.: Rupture of the Uterus in Cesareanized Women—With Report of a Case Rupturing at End of Eighth Calendar Month, *Illinois M. J.* 47: 39-41, 1925.
- White, Robert R.: Rupture of the Uterus—a Study Based on Maternal Deaths in the State of New Jersey, 1937-1941 (Maternal Welfare Article Number Seventy-Two), *J. M. Soc. New Jersey* 39: 446-449, 1942.
- Williams, J. Whitridge: Repeated Cesarean Section, in *Obstetrics, A Textbook for the Use of Students and Practitioners*, ed. 6, New York, 1931, D. Appleton and Company, pp. 553-556.
- Woodward, H. L., Bryant, R. D., Garber, S. T., and Fleming, J. G.: Rupture of Uterus, *J. Med.* 20: 106-109, 1939.

Discussion

DR. WILLIAM H. VOGT, St. Louis, Mo.—In a recent review of the statistics of rupture of the uterus, Bill and his associates mention a low incidence of 1 in every 2,260 deliveries as reported by Stander and a high incidence of 1 in 220 cases as reported by Whitacre and Fang from the Peiping Union Medical College. This great variance prompted me to look up our own records at St. Mary's Group of Hospitals in St. Louis. My object of briefly reviewing our cases is to prove that previous cesarean section and other operative procedures are the causes of most of these accidents.

In one institution we had 4 ruptured uteri of 15,498 deliveries, an incidence of 1 in 3,874 cases. There were two cases of rupture of the uterus following the classical cesarean section in both of which the rupture was found at the site of the original uterine wound. Supravaginal hysterectomy was done in both instances with the death of one mother and both children.

There were two cases of rupture following version and extraction. In one of these cases several doses of pitocin were given to induce labor. Membranes ruptured spontaneously, and immediately thereafter fetal heart tones were not heard. Manual dilatation was done followed by podalic version. The child was born dead. Diagnosis of rupture was not made until manual removal of the placenta was attempted. The second case was one of mentoposterior presentation with a Bandl's ring. Again manual dilatation and version and extraction were carried

out. Diagnosis of rupture was not made until manual removal of the placenta was attempted. There had been no shock and no hemorrhage.

In another hospital, there were two ruptured uteri at term in 7,000 deliveries, an incidence of 1 to 3,500. One case followed version and extraction in the presence of a Bandl's ring. The other case of rupture followed forceps delivery in an infected case, the patient dying twelve hours after delivery with the rupture unrecognized. In reviewing the history of this case it was found that this woman had had an operation for the repair of a rectocele and a Manchester operation four years previous to this confinement. It is quite possible that the cervical amputation was a factor in preventing proper dilatation of the cervix and resulting in the rupture.

That previous cesarean section is a great factor in the production of rupture is clearly shown in Dr. Lynch's Table II. Eleven, or 25 per cent, of his forty-four cases followed previous section. In my own records two cases followed previous cesarean section. We are all aware that a weakness of the uterine wound occurs at times following incision into the uterus and that this weakness may be expected, particularly if the postoperative course has been febrile. But even when the postoperative course is perfectly normal, rupture at the site of the previous incision into the uterus may occur.

Dr. Lynch states that an "ideal" result in the uterine wound is a complete regeneration of the muscular tissue but that this does not always take place. It is estimated that about 4 per cent or 5 per cent of cesarean wounds rupture. There is still considerable dispute as to whether the wound heals by muscle fiber regeneration or by scar tissue. It seems to me that the important principle in the performance of a cesarean section is the meticulous suturing of the wound without the constricting of tissue but at the same time closing the wound so carefully that the formation of hematoma is avoided. If this suturing is well done, it is my opinion that the wound will heal firmly and there will be little scar tissue. I base this opinion on my own observations of rarely having seen a scar in the uterus when there had been no infection and the operation had been performed by a competent surgeon.

I was glad to hear that Dr. Lynch does not adhere to the dictum, "once a cesarean, always a cesarean." I agree with him when he says that the success or failure depends on the competence of the uterine wound and since there is no reliable criterion upon which this decision can be made, it is desirable in the conduct of these cases to consider any departure from the normal or the appearance of any untoward symptoms as being those of rupture or beginning rupture and to open the abdomen immediately.

Cesarean sections are undoubtedly being done too frequently and it is my conviction that if the obstetrician would show more concern regarding the dangers to the woman and the future consequences of the first operation and would hesitate less about doing the second section, the incidence of rupture would decrease materially. Naturally, no woman should be allowed to labor after a previous cesarean section if that operation was done for a definitely determined contracted pelvis. On the other hand, if the previous section was done for other causes and there is no history of infection, the patient may be watched carefully during labor. A weakness of the uterine wound at the time of contractions can usually be detected and, in such an instance, another section should be immediately arranged for.

In the majority of cases of rupture the most satisfactory method of treatment is supravaginal hysterectomy, not forgetting the value of immediate blood transfusion. There are a few cases that might lend themselves to the repair of the tear itself after the abdomen is opened, but I rather think that this would be more time consuming than the hysterectomy, and since most of these uteri are infected or potentially so, the risk would not warrant that procedure.

Prophylaxis is the all-important point. If the patient has had a previous section, this should put the obstetrician on guard and should make it imperative that he watch for any weakness in the uterine wall. A section should be done upon the slightest indication of this weakness. Abnormal presentations should be corrected, if possible, during pregnancy. Transverse presentations, if recognized early in labor, should be delivered by version and extraction before the rupture is imminent. When version and extraction is indicated, it must never be done unless the cervix is fully dilated, and deep surgical anesthesia must first be established. Attempting to turn a baby in an unrelaxed uterus is one of the most frequent causes of rupture when version is done.

While rupture of the uterus is of comparatively rare occurrence, all statistics seem to show clearly that the catastrophe occurs most often after cesarean section and version and extraction. With our present knowledge of obstetrics we should be able to reduce the number of these accidents, but modern obstetrics in the minds of many men means operative obstetrics and operative interference, as so clearly shown in this paper as well as in other statistical studies, too often ends in tragedy. Some one once said, "We need more good obstetricians and less operators."

DR. FRANK E. WHITACRE, NEW ORLEANS, LA.—We reported forty-four consecutive cases of rupture of the pregnant uterus from the Peiping Union Medical College, China, occurring between the years 1934 and 1941.* In regard to obstetric patients admitted, this gives a hospital incidence of 1 in 95 cases, which is the highest that has come to my attention. Thirty-eight of these forty-four patients were seen for the first time as emergencies.

The most important causes of rupture of the uterus in this series were contracted pelvis and transverse presentation of the fetus, which accounted for about 50 per cent of these accidents. Twenty-five of the forty-four mothers died, and only three babies lived, but in viewing these deaths one should take into consideration the desperate condition of these traumatized, infected patients when first seen. Phlebitis or thrombosis was only suspected to have occurred once in this group, which emphasizes the rarity of phlebitis in the Chinese people.

During the last six months of 1940 and the year 1941 we treated eight patients with rupture of the pregnant uterus, six of whom recovered, and we believe that certain improvements in the management of these neglected patients accounted for the 75 per cent salvage.

We adopted an operating room arrangement for obstetric or gynecologic laparotomies used in certain European hospitals. The lower third of the operating table was removed and the patient's thighs placed in leg holders with the knees widely separated. An assistant, standing between the patient's knees, can be of much help during the operation in aiding in the identification and repair of bruised and torn pelvic structures.

Many tears in the usually infected uterus are an extension from the cervix. When applicable, we repaired the tear in the lower uterine segment and cervix first and then did a supravaginal hysterectomy. Removal of the cervix is not urgent and it is often better not to extend the operation by including it. Finally, a tube is passed through the cul-de-sac into the vagina to provide dependent drainage. The position of the patient and that of the assistant make this procedure quick and easy. In some of the less traumatized patients the tear can be repaired without removing the uterus. This is especially true of rupture of a cesarean section scar. Fluids, including blood transfusions, were liberally used before, during, and after operation. We believe that the decrease in the fatalities in these desperately ill patients was due to four factors: (1) blood for transfusion was more readily available because of the use of stored blood; (2) the use

*Arch. Surg. 45: 213-234, 1942.

of the sulfonamides must have aided materially; (3) decompression of the gastrointestinal tract, in which care was taken to maintain the blood chloride level, was beneficial; and (4) as nearly as possible, uniformity of operative technique was insisted upon.

DR. SAMUEL A. COSGROVE, JERSEY CITY, N. J.—In a rather hasty résumé of our experience with rupture of the uterus, we found that we have records of thirty-two ruptures in a series of almost 67,000 live births. That is an incidence of approximately half that of the essayist. Of these, twenty-one mothers recovered and eleven died, a mortality of 34 per cent. Nine of the babies lived, twenty-four died, a mortality of 75 per cent for the babies.

The causes of the largest group were rupture of old cesarean scars—nine, approximately 28 per cent, nearly the same as the essayist's. The next largest group were incident to version. The third largest group was due to manual or instrumental removal of secundines, really perforations of the uterus. One case followed previous gynecologic operation; I believe a suspension of the uterus.

In the treatment, six of the ruptures were conservatively repaired, two patients died unoperated, and in the remainder hysterectomy was done. These were a somewhat diversified group, the largest proportion of which represented tears of the cervix into the lower uterine segment and broad ligaments. It is significant, it seems to me, that the entire mortality occurred in ruptures of the lower uterine segment. This is partly because of the relative difficulty of recognizing these cases as ruptures, as the essayist has pointed out, as compared to the somewhat dramatic and clear-cut syndrome represented by bursting of the corporeal segment.

The danger of version under improper conditions, as represented in this series, is of importance and should be stressed.

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD.—We have recently reviewed our cases of rupture of the uterus at the Johns Hopkins Hospital, some of our findings being as follows: Among some 53,000 deliveries at Johns Hopkins we have had a total of fifty-three ruptures of the uterus, an incidence of 1 in a thousand. There were ten ruptures of cesarean section scar and forty-three cases of noncesarean ruptures. There were seventeen spontaneous ruptures and twenty-six traumatic ruptures. One of our findings had to do with the important role played by age and parity in spontaneous rupture of the uterus. Among seventeen cases of spontaneous rupture, the average age of the patients was 36.3, and the average parity, 6.4. All of the patients were multiparae. This suggests that the primiparous uterus is more or less immune to rupture and the multiparous particularly vulnerable. The age incidence also suggests that senile changes take place in the uterus which make women in the upper-age and parity brackets especially susceptible to this accident. Further intimation that there is some inherent defect in the uteri of these older multiparae is found in the brief period of labor preceding rupture, the average being 12.8 hours. The babies tended to be large.

As Dr. Lynch pointed out, rupture of the uterus is often overlooked and in six of our cases vaginal delivery was carried out without realizing that rupture had previously occurred. In eight cases the diagnosis was made only post mortem.

How often do cesarean section scars rupture? We have had under our care 624 patients who have had previous cesarean sections and whom we have carried through pregnancy and delivery. A repeat cesarean section was done in one-half of these patients because of disproportion plus scar. In 20 per cent we did cesarean section simply because of fear that the scar would rupture, and in 30 per cent we have carried them through delivery. In this series the incidence of rupture of the cesarean section scar in pregnancy or labor was 2 per cent.

In our experience, as in others, the most common cause of traumatic rupture has been version and extraction.

DR. E. L. KING, NEW ORLEANS, LA.—I notice that the administration of pituitary extract is only mentioned incidentally as a cause of rupture of the uterus. We warn against the use of pituitary even in small doses. I can recall three cases of rupture, one of which occurred in the hands of a midwife before admission to the hospital. Another case occurred in my service at the Charity Hospital, in a multipara, in an attempt to speed up a very slow labor. Two minim doses of pituitary extract were given at intervals of two or two and a half hours and the patient died. I had one patient about a year ago whose membranes had ruptured at seven months and labor had not ensued. I had tried medical induction, then put in a bag and nothing happened. Although I am very much afraid of pituitary extract, I gave her three one-minim doses and nothing happened. I then gave two minims and she developed a rupture of the lower uterine segment. So even two minims of pituitary may cause trouble.

Our policy has been to do a section always in a woman who has had a previous classical section; also if we are in doubt about the type of section that has been done previously. Where we are sure it has been a low section and there is no disproportion, we let the patient try vaginal delivery. However, I have had two repeat sections in my own private series where I found a very thin scar at the second operation which might have ruptured.

DR. B. H. CARROLL, TOLEDO, OHIO.—Dr. Lynch and Dr. Vogt do not include any cases with the diagnosis of spontaneous rupture. This indicates the careful study they have given their material. Spontaneous rupture simply means cause unknown.

I would like briefly to report a case of rupture of the uterus in the eighth month of pregnancy. At 19 years of age a primipara was delivered for placenta previa by low section. In a second pregnancy at the age of 21 she was delivered spontaneously after a ten-hour labor of a living baby, weighing 7 pounds. The placenta was retained for twenty-four hours, then expelled spontaneously, but her recovery was afebrile. Her third pregnancy one year later had been normal up to the eighth month. While sitting in a chair sewing there was a sudden, sharp, taring pain in the lower abdomen followed in a few minutes by collapse. Two hours later in the hospital a diagnosis of ruptured uterus was made. The abdomen was opened. A dead fetus of about eight months' size together with the placenta were free in the abdominal cavity. A large rent extended diagonally across the lower uterine segment, anteriorly down to the vaginal vault. Hysterectomy was done and the patient recovered.

Pathologic examination showed that the healed scar of the previous section was not involved in the rupture. Venous thrombosis and degeneration of the myometrium were present at the point of rupture. The rupture was not through the placental site, and the decidua basalis and decidua vera appeared to be normal.

The original placenta previa could hardly have damaged the vessels and muscles to such an extent, otherwise the rupture would have occurred during the second pregnancy and labor. With her second delivery the retention of the placenta for twenty-four hours might suggest a partial placenta accreta and this in turn accounts for muscle and vessel damage. Clinically, it was a simple retention of a normal placenta. In this case we are hesitant to make a diagnosis of spontaneous rupture, especially in a patient who has had the above-mentioned history. We feel that some unknown cause produced a venous thrombosis followed by degenerative changes in the muscle, making possible the unexpected rupture of the uterus.

DR. W. A. SCOTT, TORONTO, CAN.—The commonest cause of nontraumatic rupture of the uterus is the presence of a scar from a previous cesarean section. Whenever a discussion of cesarean section arises, the interests of the baby as an indication

are always raised. When cesarean section is done, and most particularly in the case of the young primipara, in addition to the immediate prognosis we must remember that her future obstetric history is made more dangerous.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—There are two symptoms in connection with rupture of the uterus which are frequently overlooked. These may be the only, or the first, evidences of rupture. The first is the intuition of the patient. She feels or hears the actual tearing of the uterus or of the uterine scar. In one of our cases this was overlooked and six hours later we discovered the rupture by examination. In this case, there was little or no hemorrhage and the fetus survived, since placental separation, for some reason, had not occurred. The other symptom is chest pain of the diaphragmatic type. In a recent case of apparently normal but slow labor, the patient began to complain of severe shoulder and chest pain. Investigation discovered nothing in particular to account for it until four hours later separation of the placenta occurred, with massive intraperitoneal hemorrhage and death of the child.

DR. MILTON G. POTTER, BUFFALO, N. Y.—Three years ago before this Association I brought forth the idea that the suturing of the uterus, whether it be in a high or a low section, in most of the cases was faulty. In other words, we were strangling tissue and we got sloughing of tissue due to the fact that we were putting in too many sutures. I also called attention at that time to the technique that we are now using a single layer of silk suture which includes only the outer third of the muscle. Our results since I reported that procedure have been most favorable, our postoperative convalescence free of trouble. While one must be meticulous with sutures, too many should not be inserted. If there is a rupture, it is usually not in the scar but alongside the scar. We believe that by use of silk sutures in the outer third of the muscle we are getting primary muscle regeneration. We are able to prove this fact by histologic slides which were prepared and studied at the Army Museum in Washington.

I would like also to say that a procedure such as version and extraction should not be condemned. It is not the procedure but the judgment of the operator that should be condemned because anyone who undertakes a procedure of that type, as a last resort—and we have so often called attention to that fact—will certainly get bad results.

UTERINE DEFENSE MECHANISM AGAINST INFECTION*

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IT WILL, I think, be generally conceded by surgeons that there is no cavity other than that of the postpartum uterus (eight to ten inches long, completely denuded of its mucosa, traumatized, ecchymotic, torn and generally wholly disfigured at its lower pole, and communicating with the surface) that could recover its normal state without a severe infection ensuing. Nature placed the outlet of this cavity at the most untoward spot on the human surface, between the outlets of the two evacuant canals, and yet the rule after delivery is an uneventful recovery and, in the vast majority of cases, a recovery and a return *ad integrum* without detectable infection. What other sinus of the body, produced even under the most complete surgical asepsis, could remain uninfected? We know that the lochia seventy-two hours after delivery is swarming with microbes, and we also know that the cervical mucosa retains its infection in 70 per cent of cases after delivery. However, the uterine cavity remains sterile under these circumstances. Or does it? And if it does not, then the infection, judging from the completeness of most recoveries, must be rendered innocuous by some unique device. Let us look at this matter in its combined scientific and clinical aspects, bringing all our knowledge to an impartial criticism. Is the uterine cavity sterile (1) in the virgin, (2) in the married nullipara, and (3) in the multipara? Cultures have proved with almost monotonous regularity that the uterine cavity in the nonpuerperal state is aseptic. But these attempts at culture have always been surrounded with insurmountable difficulties, causing breaches of technique and irrefutable objections as to their validity. The mere introduction of a cannula to withdraw contents from the uterine cavity may defeat its purpose by introducing infection and, what is of far greater importance, cultural methods of some years ago were hopelessly inadequate. Let us allow this aspect to rest.

What does clinical experience teach us? It teaches first of all that there must be many strains of chronic organisms that are viable only in the tissues and not outside of them. Therefore, to culture these would require curettings obtained from the uterus aseptically and attempts at culture from the macerated endometrium with varied media. That this would produce results in a percentage of cases I have not the slightest doubt. My reasons for this are purely clinical, but they are many. In the first place, if we take a virgin who has a catarrhal endocervicitis of long standing (this is not uncommon), we frequently find that after

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marriage she is sterile, and upon trying to determine the cause, one may find that it is due to one of two things: (1) to the endocervicitis having a deleterious effect upon the sperms or (2) to permanent or temporary obstruction at the cornual end of the tubes. In the first instance, the condition is curable by cautery; in the second instance clinical experience teaches that the cautery may improve the cornual disease in time but that it is more readily overcome by tubal insufflation. Now how is the normal patulous character of these tubes lost? Definitely by an ascending infection from the diseased cervix through the uterine cavity to the cornual constrictions. Cases of this nature have been so numerous in my experience as to leave no doubt not only as to their existence, but also as to their mode of development. Can we state under these circumstances that the uterine cavity is sterile? I have demonstrated the presence of acute salpingitis and peritonitis as a sequence to vaginal trichomoniasis and will report shortly cases of ovarian abscess in nulliparae where the fimbriated ends were free and trichomoniasis, though not demonstrable in the abscesses, infested the genital tract. Is it necessary to do more than mention the ascending character of gonorrheal infection from the cervix to the peritoneum? In a paper to be published soon I emphasized the frequency of ascending infections in puerperal cases and the slowness of their progress from the cervix through the uterine cavity and tubes to the peritoneum.

We must assume that ascending infections are much more common than we have heretofore conceded. This property of a slowly ascending infection was for years restricted to the gonococcus. Now we know that any tenacious organism can produce like results and, what is of much more importance, that they are fairly common. How frequently we see abortions follow from a diseased endometrium as a sequence to a chronic endocervicitis! And yet, in spite of these instances, we are forced to the conclusion from clinical experience, that the uterus is free from pathologic infection in the vast majority of cases and that it must have a defense mechanism which is quite special. It is with this aspect that I propose to deal at present.

Has the uterus a special defense mechanism? Yes, quite apart from the protection given to the uterine cavity by the cervix and its flow of tenacious mucus. There are at least four or five special defense mechanisms, and there is a probability that there are many more of a biochemical nature, but these, in the present state of our knowledge, are too hypothetical to warrant anything but speculation. The several known are as follows:

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| 1. Desquamation | 4. Development of mesenchymal cells in the |
| 2. Exfoliation | parametrial tissues during pregnancy |
| 3. Local lymphocytosis | (Hofbauer's cells) |
| | 5. Closure of the uterine cavity by blood clot |

1. *Desquamation*.—It need hardly be emphasized that the monthly desquamation of the uterine mucosa during the cyclic changes brings

about conditions that have been thought to weaken the defenses and to open the portals of infection. This line of reasoning is dictated by analogy of other raw surfaces, but it is not true. Careful pathologic study of uterine disease processes shows that not only is desquamation not a breaking down of defenses, but that it is a powerful means of minimizing the effects of infection when the uterine cavity has become contaminated. It is the experience of every gynecologic pathologist who has given this matter study that any acute ascending infection affects the different parts of the genital tract in quite different degrees and with quite different end results. Let us take acute gonorrhea in the female as a well-known example. The vagina, owing to its squamous covering and its freedom from glands, like all squamous surfaces is practically invulnerable to the gonococcus. One may find a vaginitis with gonorrhea, but it is chiefly of an irritative type due to toxic secretions and yields promptly to cleanliness. With the cervix uteri, on the other hand, the course of this infection is quite different. In the cervix we find a columnar surface with numerous racemose glands. Infection will persist for long intervals, months and possibly years, in these tissues, showing a widespread lymphocytic and leucocytic infiltration of the submucosal areas and occlusion of the cysts of Naboth. There is a tendency of late to decry the tenacity of the gonococcus and to attribute the continuance of the infection to reinfection from coitus. That is merely denying the tenacity of the gonococcus in the female and asserting its tenacity in the male, which is hardly logical. There came into the orbit of my experience, two cases of young newly married nulliparous women who contracted gonorrhea from husbands fairly recently infected. The two cases ran almost parallel courses. The infection rapidly ascended and each woman developed a choked pelvis. These women were continuously in hospital, one for three and one-half months, the other for five months, when every known form of treatment was carried out. Finally it was decided to operate and remove everything down to and including the cervix. There were pus tubes, ovarian abscesses, etc. Now, intercourse had been impossible under these circumstances, yet gonococci were demonstrated in the secretions of the cervix and pus tube in the one who had been hospitalized for five months. But the interesting feature of these cases was the vast difference in the effect of this disease upon the different parts of the genital canal. The cervix was badly infected with all the signs of a subacute infection, including infected nabothian cysts. The tubes were so broken up with inflammation and pus that they had lost most of their character. But the uterine mucosa showed nothing but a few small surface areas of lymphocytes and polymorphonuclears—a pathologic condition that was so slight that it might easily have escaped observation. The contrast was most striking. How can we explain it? Well, it is generally contended that pus tubes are retention cysts due to bad drainage. Perhaps that is the whole truth regarding the tubes, but how can the tenacity

of the cervical infections as contrasted with the paucity of signs in the uterine cavity be explained? This cannot be explained by the lack of drainage, for the cervical canal is in a better stage to effect its drainage than is the uterine cavity. The question revolves about the cycle of menstruation with the shedding of the superficial layers of the uterus and the outpouring of its blood and of its biologic secretions. The function of menstruation is a protective one as regards infection and tends to renew the uterine mucosa and keep it young and healthy for the preservation of the race.

2. *Exfoliation of Puerperal Products in the Uterine Mucosa.*—In 1912 I published a monograph upon the involution of the puerperal uterus entitled "Studies from the Royal Victoria Hospital" in which was described how the large subplacental vessels of the uterine wall undergo degeneration and absorption to be replaced within their lumen by a new vessel commensurate with the reduced size of the uterus. It was also pointed out that *complete* destruction and absorption of these superfluously large vessels was a rare occurrence and happened only under optimal circumstances of age, health, and normalcy of the puerperium. Therefore, almost every parous uterus carries scars in its walls of previous pregnancies. Williams, in 1928, carried my work further and discovered that these large vessels in the musculature of the uterus underwent the changes that I had described but that the truncated ends of these vessels in the uterine serotina were not absorbed but were severed at the musculomucosal junction, and that the distal mucosal sequestrum of each of the obliterated vessels was gradually exfoliated by the new mucosa which grew under it and gradually pushed it out as a foreign body. It takes from two to three months post partum for this exfoliation to complete itself. I have had ample opportunity to observe the correctness of this teaching and in two cases, one six weeks and another two months post partum, puerperal hemorrhages almost lethal in character occurred, requiring transfusion, and digital exploration revealed a hard spicule in the placental site of partially exfoliated dead or dying blood vessels. I had occasion also in several puerperal hysterectomies, performed several weeks after labor, to verify Williams' discovery. Now, the reason for the exfoliation is to preserve the endometrium healthy and intact, free from scars such as are found in the uterine musculature. One can well imagine the effect of a large number of pregnancies upon a uterine mucosa if left its quota of scar tissue. Nature is very prolific in her resources in reverting to the normal, especially when it involves the preservation of the race. If the uterus retained its pregnancy scars in the mucosa, we would have numerous loculi of lowered resistance against infection and a multiplicity of complications that would make the placental separation extremely difficult.

3. *Local Lymphocytosis.*—The third mode of defense is lymphocytosis. A great deal has been written about the lymph nodes of the uterine

mucosa, but no one, so far as I know, has ever advanced any reason for this condition. And there must always be a function to explain the persistence and maintenance of any natural biologic structure. Otherwise it would quickly disappear. That is merely the law.

The lymph nodes of the uterine mucosa are found in the deepest layer of the mucosa, the layer that undergoes the least changes in the menstrual cycle and is not shed at menstruation. This layer seldom responds to the effects of estrin and progesterone and is more or less stable. One sees the conservatism of nature in placing the lymph nodes in this permanent layer. I have found nodes very rarely in the superficial layers of the mucosa and then only in definite pathologic states. The nodes are of two kinds. They differ, not in the contents, but in the arrangement of the lymphocytes and matrix which constitute them. In the first type the node is clearly circumscribed from the surrounding stroma of the endometrium and the deeply staining blackish lymphocytes are uniformly spread throughout the nodule. On careful focusing one can see the large granular matrix cells among the lymphocytes, but they are not striking. On casual examination the condition resembles merely a mass of lymphocytes. In the second type the lymphocytes are all about the periphery of the node, and the central zone is made up of large plasma cells of enormous proportions with vacuolation and fragmentation of the nuclear chromatin and scattered cavities, as if a soluble substance had been removed. These two pictures are but two phases of the same structure. These two phases are also met in the lymph nodes of the appendix and spleen.

Now we come to the question, What is the function of these lymph nodes? After careful study of endometrial lymph nodes and of those of other parts of the body, one is forced to the conclusion that one of their functions, if they have any other, is protection against infection. They are the watchdogs of protection. The lymphocytes are elaborated in the lymph nodes and are wandering cells, nonphagocytic; they wall off any foreign invasion and isolate it. One sees the lymphocytes at times as fine black dots scattered throughout the uterine mucosa. At other times they are confined exclusively to the nodes. From careful observation they do not take any part in the cyclic changes. But in cases of chronic infection the nodes may be greatly increased in number so as to fill the microscopic fields. As in the appendix, where many of the lymphocytes pass out of the tissues into the lumen of the appendix, so also do they wander into the glandular lumina of the endometrium and ostensibly are lost to the economy, though there is no proof that they cannot equally easily wander back again. An interesting feature is that so far as my research has gone, the lymph nodes do not appear in the uterus until puberty. Nodes are not found normally in the cervix, nor do they appear there except as a response to subacute or chronic infective agencies. But in the cervix the arrangement

described does not appear in anything like the regular phases found consistently in all uterine mucosae.

What are the inferences? If we examine the distribution of lymphoid nodes throughout the body, we are struck by one great generalization—these are outposts of the master organ of lymphocytosis, the spleen—and are placed by nature at weak spots of infective entry into the body economy. The distribution of lymph nodes corresponds exactly to the correct distribution of military forces in a hostile country. The weakest defenses of the body are also the economy's chief concern. These weak spots are the food portal, the air portal, and the procreative portal. The surfaces of the body are protected by their thick imbricated layers of squamous cells. This protective coat against the contacts of life has hardened, as the bark of a tree, chiefly by the effects of "water balance," as the scientists put it. And this reinforcement of skin has its drawbacks also (mainly it limits absorption) so that the chief requisites of the body have to be absorbed through a more delicate lining, hence the delicate mucous membranes of the digestive, respiratory, and genital tracts. But, owing to this weakness of structure, there is a corresponding weakness in the defense mechanism. These tracts are really extracorporeal in the sense that they communicate with the exterior, and bodies occupying them are really not intracorporeal until they are absorbed through the delicate mucous membranes that line these cavities. To protect against foreign entries nature has placed lymphoid tissue as outposts, and the amount and number of these correspond to the degree of danger and amount of absorption. This balance has been developed through the degree of exposure to the danger during the aeons of evolution. One can see in this evolution an efficient and ready means to meet an inimical invasion. We know that the spleen is the headquarters of lymphocytic elaboration. But valuable time would be lost if there were but headquarters. Nature, however, has placed in these outposts small, efficient spleens proportionate to the danger—large in amount in the throat, scanty in the stomach (owing to the sterilizing effect of hydrochloric acid) most abundant where absorption is maximal (namely, along the ilium and cecal region). Because the uterine cavity communicates with the exterior, it has established its own outposts to give as ready response as possible. The number of lymph nodes in the mucosa varies within wide limits in different individuals and in different species. In one of my patients the mucosa was so filled with normally constructed lymph nodes that they quantitatively outspaced the mucosa proper. This was due to a chronic local infection of long duration.

4. *Cellular Reaction in the Parametrium.*—In 1926 Hofbauer published a work upon the cellular reaction in the base of the broad ligaments during pregnancy and puerperium. This reaction consists in the presence of two types of cells in the lymph spaces. These are the clasmatoocytes and the monocytes. Later, a third cell was defined which

became the stem cell, of which the two former are developmental forms. All three varieties are of mesenchymal origin, due to some reaction during pregnancy. The condition becomes more marked after a prolonged labor or in the presence of infection. These cells are found more numerous in the paracervical areas and are markedly phagocytic.

Hofbauer states: "What is the influence, it may be asked, which, during pregnancy, causes the development in the parametrium of a phagocytic tissue which is evidently intensified under the stress of labor? Since for the last few years pathologists emphasize that due to irritation by foreign protein substances in various organs there is a response of mesenchymal tissue elements and of undifferentiated cells in the immediate vicinity of blood vessels, our attention was first of all directed to a causative factor of this kind. There is, however, nothing which leads us to believe that the specific stimulant in the parametrium is the result of the breakdown of fetal or chorionic tissue. It is unlikely that the well-known proliferation and breaking off of buds of chorionic tissue into the maternal blood stream—the so-called deportation—can be considered the main factor; particularly as this is most marked in the early stages of pregnancy, while the parametrial changes attain their highest development at its very end. On the other hand, it is conceivable that the hormone, or whatever substance it is that produces the well-known changes in various organs of the pregnant woman, causes the parametrial phenomena."

5. *Closure of the Uterine Cavity by Blood Clot.*—Recently we had the misfortune to lose a patient post partum, and I had to do a hysterectomy post partum on another patient for torsion of a pedunculated fibroid. The careful study of these two cases has given us much data upon the defensive measures of the uterine cavity. In the autopsy case, in which the patient died on the third day post partum of pulmonary edema from advanced mitral disease, the pelvic organs were removed very gently en bloc. It was my conception before investigating this case that the evacuated uterus remained a cavity, because when the post-partum uterus is invaded by hand or instrument for whatever cause, it gives the impression of being just a muscular bag. That is not true, however. It was found that the anterior and posterior walls of the uterus were agglutinated by a thin layer of clot which ceased to be adherent at the lower margin of the upper uterine segment. The clot projected through Bandl's ring as a blunt obturator, as any clot will do if it forms at the end of a tube. So intimately were the two uterine walls bound by the clot that microscopic sections were made of the two walls and the intervening clot without disturbing the normal relations.

The study of the renewal of the new mucosa underneath this thin but extensive layer of clot and blood-permeated redundant tissues is a vast and interesting new field for future description. Suffice it to say that in normal noninfected patients most of the lochia of the first few days comes not from the uterine cavity, but from the tip of the plug at the lower uterine segment and from the traumatized and regenerating tissues of the lower uterine segment and cervical and vaginal canals.

Only later does lochial discharge come from the uterine cavity, when the clot has served its sealing purposes and is being disintegrated in the regeneration of the uterine mucosa.

The second case came under study following a total hysterectomy in the fifth day post partum. Here again the main features of the process of protection by clot and repair were corroborated. It becomes quite clear, in view of these disclosures, why the uterus, unlike any other surgical cavity, so frequently escapes infection. It is because it is not a real cavity but only a potential one. If it were not for this sealing of the uterine cavity, few women would escape puerperal infection. Retention of large strips of membranes or portions of placenta would prevent nature's effective closure of the uterine cavity by clot, leaving a cavity and a wick for the entry of infection. Conditions for normal regeneration of the uterine mucosa are limited. The blood clot must be minimal but sufficient to cause effective closure of the uterine cavity. Excessive clot is detrimental in the same degree that an optimum amount of coagulated blood or serum is necessary for the healing of any wound. Any amount above this is correspondingly detrimental, causing, when largely excessive, breaking down and producing conditions conducive to infection. Normally the two opposing walls of the uterus, the anterior and posterior, are joined post partum by a minimum of clot which, in the parts nearest the torn mucosa, acts as a bridgework for regeneration of mucosal elements. Any spontaneous invasion of the uterine cavity by infective agents from below would have to overcome the normal barrier of this thin clot before reaching the viable, vital parietal tissues.

It is my impression that this sealing off of the uterine cavity is the most important of the protective agents in the postpartum recovery. That the medical profession has felt this for years is shown in the care of obtaining a complete removal of placenta and membranes and in the anxiety which follows any retention of these in any patient under observation. Though the cause for anxiety arose out of a possible infection following upon such retention, the basic reason lay in the fact that the uterine cavity, under these abnormal circumstances, became a real, not a potential, cavity.

Conclusions

It has been shown that many factors enter into the protection of the uterine cavity against infections. Among these are five that are of first importance. These are chiefly mechanical. It is probable, even certain, that many other biochemical agents enter into this protective shield.

The five enumerated are as follows:

1. Desquamation
2. Exfoliation
3. Local lymphocytosis
4. Development of mesenchymal cells in the parametrial tissues during pregnancy (Hofbauer's cells)
5. Closure of the uterine cavity by blood clot

The fifth one is now elaborated, I think, for the first time. It consists in a sealing off of the uterine cavity by blood clot and the growth of a new mucosa under the bridgework, just as an open wound on the surface or an incision is sealed by an optimum minimum of extravasated blood.

When completely closed off, the major part of the lochia comes from the lower uterine segment and from the serum squeezed out of the uterine cavity during the early days post partum and from the disintegration of the uterine fibrin after it has fully discharged its function.

References

- Goodall, J. R.: The Involution of the Puerperal Uterus. Studies from the Royal Victoria Hospital, Montreal, 1922.
 Hofbauer, J.: The Defensive Mechanism of the Parametrium During Pregnancy and Labor, Bull. Johns Hopkins Hosp. 33: 255, 1926.
 Williams, J. Whitridge: Regeneration of the Uterine Mucosa After Delivery, With Special Reference to the Placental Site, AM. J. OBST. & GYN. 22: 664, 1931.

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Discussion

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—Dr. Goodall's interesting presentation opens up a wide field of speculation as to the reasons for the comparatively enormous resistance to infection which results from what must, in most instances, be a considerable trauma associated with delivery. The fact is generally acknowledged but there is no certainty as to why this should be. Puerperal infection is often a tricky phenomenon, whether endogenous or exogenous, if that distinction is always possible. It may not occur in cases where it is most feared and again in others where there seems to be no reason apparent. The probability of the occurrence of puerperal infection in any individual case has developed into the general conclusion that prophylaxis constitutes the all important factor.

The contagiousness of this complication of pregnancy was demonstrated satisfactorily enough by White in 1793 and by Gordon in 1795, more completely confirmed by both Holmes and Semmelweiss independently between 1840 and 1845. These discoveries were neglected, however, until Lister some thirty years later placed the matter on a more scientific basis by showing that bacteria were the causative agents in wound infection. Finally, Pasteur and Doloris demonstrated that streptococci were present in the uterus in cases of puerperal fever, demonstrating that the disease was closely related to suppurative processes. While this accumulating but frequently disputed knowledge did finally result in a reduction in the mortality of childbirth, which is no longer appalling and rarely takes on the picture of an epidemic, the fact still stares us in the face that it has not been eliminated and that perhaps 25 per cent of the puerperal deaths are due to infection. Therefore, a further inquiry into the etiology such as that presented by Dr. Goodall is not only of theoretical, but also of practical interest and importance.

The presence of infective organisms in the uterus and adjoining pelvic structures is or must be assumed, whether inherent or accidentally introduced. If their growth or distribution during labor or soon after is inhibited, the reasons should be sought for. Hofbauer, in 1926, directed attention to the presence of accumulating fibroblasts in the parametrium where it approaches the uterine walls and said that these become more abundant in the presence of early infection. He believed that these act as macrophages which ingest and destroy the invading bacteria and also in-

crease the immunity. Stieve, in 1929, confirmed these observations and the fact that histologic changes in the uterine connective tissue of an embryonic type act with a similar function. Louros, Scheyer, and others then claimed that the reticulo-endothelial system constituted a secondary line of defense, while Miller and Whitaker at the same time showed that the antibactericidal power of the blood progresses with pregnancy. All of these theories agree more or less, but the picture is by no means complete and the claims put forward by the reader of this paper must therefore be accorded deserving attention.

Goodall emphasizes the importance of the closed postpartum uterine cavity due to fibrinous agglutination of its walls after the placenta is delivered and the adverse results which develop when this process is interfered with. In addition, there is the proper healing of the denuded mucosa under this protective covering. Perhaps this is nothing more than the regeneration which ordinarily takes place under a "scab" or the desquamation during menstruation. The association must yet be proved more adequately, and undoubtedly the proof or disproof eventually will follow.

In the meanwhile it would seem desirable that whatever practical lessons may be learned from these observations of Goodall and those who preceded him be concentrated on the need for adequate obliteration of the uterine cavity after delivery by oxytocic measures. It may be that the antihemorrhagic use of ergot, pituitrin, and similar preparations has had an equally deterrent and inhibitive effect on preventing puerperal infection. However, I believe that further investigations to halt, or, better, to prevent this crippling or fatal complication of pregnancy should be developed. In the meanwhile the theoretical explanation advanced by Dr. Goodall should be given due and full consideration and his promise of further observations should be encouraged.

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—For many years my personal view about puerperal infection has been that if a woman could take care of the germs that were in her vagina, it was up to me not to put any new ones in. I have also believed that puerperal infection is an ascending affair and I am convinced that the ascending infection is through the lymph channels. If you keep the channels closed, you will not get ascending infection from the germs a woman has.

When doing home obstetrics it was my practice to keep the uterus firmly contracted. I do not believe that single large doses of an oxytocic substance will keep this contracted long enough. It seems preferable to develop a technique of keeping blood clots out of the uterus rather than squeezing and massaging it after they have formed. For that reason I feel that Dr. Goodall has instituted a scientific investigation which will be of inestimable value.

THE WERTHEIM OPERATION FOR CARCINOMA OF THE CERVIX*

JOE V. MEIGS, M.D., BOSTON, MASS.

(From the Vincent Hospital Wards of the Massachusetts General Hospital)

I PUBLISHED a paper in 1944⁴ giving a résumé of my attempt to use the Wertheim operation as a means of treating cervical cancer. Another year has gone by and because more time has elapsed, a more satisfactory study of the cases can now be presented. The larger the number of cases operated upon and the longer the patients are followed, the more satisfactory the operation seems to be. It is obvious to me that advanced cases are not to be included and that age and general physical condition are important in the choice of patients for treatment.

The argument for the treatment by surgical means bears repetition, and the five reasons that comprise the argument are as follows:

1. If the cervix has been removed, there is no chance for a recurrence in it.

2. If the cervix has been removed, no cervical cancer can regrow in it as a recurrence.

3. Certain cancers of the cervix are radiation resistant, a fact proved at the Pondville Hospital, where multiple biopsies are performed at the time the x-ray and radium treatment are being carried out.

4. There will be less damage to the bowel if surgery is undertaken. Lately, forty-six cases of serious bowel injury have been found in our clinics.

5. From the work of both Bonney¹ and Taussig⁵⁻⁷ it is obvious that patients with lymph node metastases can be cured by surgery in some instances, and this author believes that it is not possible to cure with radiation cancer in lymph nodes deep in the pelvis.

Studies of the vaginal smears in patients four and five years after radium treatment occasionally show cells in the vaginal smears that suggest a recurrence of the cancer or a persistence of it. The not too infrequent finding of a recurrence five to ten years after radiation suggests that either the tumor was not eradicated or that, following radiation, a new tumor occurred, either because the cervix had been retained or possibly because the radiation itself was responsible as the etiological factor. It is definitely conceivable that radiation itself may, by its carcinogenic action, produce a new tumor. It is interesting that vaginal smears in cases operated on by the Wertheim method have been negative; the cells so frequently seen following radiation are not present. In histologic

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preparations, cancer cells following irradiation are seen completely surrounded by connective tissue and are imprisoned. It is conceivable that clumps of cells may occasionally break through to the surface and be shed into the vagina. The observations noted during the study of vaginal smears present a new and sixth reason for advocating radical surgery. With the cervix removed, it cannot become the nidus of a recurrence or new tumor.

The material for this report was obtained from three hospitals and the author's private practice. The first case was operated upon in February, 1939, and the last one in this series in June, 1944. The total number of cases is now sixty-five. In the last report a group of nonelective cases were included that were operated upon because of the failure of radiation therapy; in this study this group has been eliminated. Thirty of the patients were operated upon at the Pondville Hospital, thirty-two at the Massachusetts General Hospital, and three at the Palmer Memorial Hospital. In the year 1939, two patients were operated upon; in 1940, eight; in 1941, eight; in 1942, nineteen; in 1943, eighteen; and to June, 1944, ten. The group is not great and it constitutes about 15 per cent of the total number of patients with cervical cancer seen, which is the usual percentage of early cancer in a large series of patients. In any group of early cases there are those who are old and those in poor physical condition, and they are not included in the operative group. The ages of the patients are of interest. Fifty of them were 49 years of age or younger, and fifteen, 50 years of age or older. Most of the patients were between the ages of 30 to 50 years. All patients have had a microscopic diagnosis of carcinoma made upon their tumor. None of the biopsies at the time of operation were reported as carcinoma "in situ," "precancerous," or "intra-epithelial." Some tumors have been much more advanced than others, but in nearly all instances a real and easily visualized cancer was present.

Selection of Cases

The patients selected for surgery should be young, preferably below 50 years of age, and in good physical condition. It is important that they are thin; patients of moderate size may be chosen but obese women should not be chosen. The tumor may involve the cervix in part or entirely; it may advance upon the vaginal walls to not over 1 cm. from the cervix. The reason for this is that it is difficult to remove enough vaginal cuff if the tumor has advanced onto the vagina. In such cases the vaginal lymphatics are infiltrated with cancer, which cannot be seen or felt. Vaginal extensions may be easily removed but it is to be doubted if they can be cured by surgery. The cervix should be movable, as felt by vagina and by rectum; fixation must mean infiltration beyond the cervix, and, although the lesion can be removed, lymphatics full of cancer cells cannot. Palpation of lymph nodes in the iliac, ureteral,

or obturator regions is no excuse for not operating if the other reasons for selection are satisfactory. It is exactly such patients that we hope to cure by means of radical surgery. Distant metastases or isolated low vaginal metastases certainly rule out any attempt at cure. If pyelography demonstrates that the ureter is dilated but the lesion seems operable, the patient should be given the benefit of the doubt, for surgery may cure such a patient if the block in the ureter is due to pressure of a node.

The Operation

The operation is the classical Wertheim or Clark operation, if we understand that operation to mean a complete dissection of the pelvic lymph nodes from the bifurcation of the aorta down, plus the removal of the cervix, vagina, and parametrium. I believe the Wertheim-Clark operation is not so complete, so I prefer to call this operation the Wertheim-Clark plus the Taussig operation—the pelvic lymph node dissection as advocated by the late Dr. Fred J. Taussig. The dissection starts along the common iliac artery and includes a dissection of the nodes and fatty tissues about it and the internal and external iliac arteries and veins. The obturator foramen and nerve are cleanly dissected and the ureter isolated from the region of the common iliac artery to the bladder. The ureter *must* be protected as far as possible. In the first operations the ureter was bared from the bifurcation of the common iliac artery to its entrance into the bladder. At the end of the operation the ureter looked like a wire suspended across the deep pelvis. At the present time an attempt is made to keep the ureter attached to the peritoneum medially. Just above the first real branch of the internal iliac or hypogastric artery, there are a very small artery and a vein which arise from the internal iliac artery and vein to give blood supply to the ureter. Great care must be taken to preserve these vessels. This blood supply was drawn to my attention by Dr. James M. Neil of Oakland, California, who has been visiting and studying at the Massachusetts General Hospital. At autopsies on the female he has dissected out the blood supply of the ureter and has convinced me that I have severed this important blood supply many times. Inasmuch as the next important blood supply to the ureter arises from the uterine artery as it crosses the ureter and must be sacrificed, it is obvious that the ureter may be without satisfactory blood supply for too long a distance if the small artery from the hypogastric is severed. A sufficient number of cases has not been done to prove this point, but it is the most intelligent hint I have encountered in connection with ureteral injury. The dissection of the obturator foramen is easily accomplished and in this area more positive nodes were found than in any other area. This dissection can be started by blunt scissor dissection and during the dissection great care must be taken not to injure the many veins that lie in the base of

the foramen, for these veins are of good size and bleeding from them is difficult to control. Separation of the rectum from the posterior vaginal wall tests the surgeon. There are many great veins and arteries in this area and care must be taken to keep blood loss during this part of the operation at a minimum, for this part is at the end of the operation and shock may be impending, and blood loss is therefore extremely hazardous. The separation of the rectum from the vagina is very similar, except much more extensive, to the separation of the posterior vaginal wall from the rectum during posterior colporrhaphy. A good line of cleavage can be found for part, but not all, of the dissection. It is well to suture the vaginal cuff with a hemostatic stitch in a circular manner to check bleeding from the vaginal veins. The vagina is left open and not closed, to allow for adequate drainage from the pelvis. No drains are used as the open vagina suffices. No attempt is made to suspend the vagina or to close or stitch any of the pelvic structures together. The peritoneum is closed with a running catgut stitch, starting from a corner near the common iliac artery and continuing around the pelvis to the other side. In our follow-up we have not seen a prolapse of the vaginal vault. The vagina is short but always well held up. The duration of this operation varies from one and a half to two and a half hours, and it is well to have the patient given a continuous intravenous clysis of saline solution, and toward the end of the operation a blood transfusion is given. In every instance the patient is prepared for two to three days with 6 Gm. of sulfadiazine daily, and after the operation sulfadiazine is given intravenously until it can be taken orally. Sulfadiazine is given for five to six days after operation. The use of sulfanilamide in the pelvis and under the peritoneal flap has been abandoned as we feel it is not necessary, and because of the possibility of foreign body reactions about the sigmoid. It is interesting to note that none of the sixty-five patients prepared this way has had general peritonitis, which has always been the great danger from this type of radical surgery.

Complications

The only really serious and annoying complication is damage to the ureter and consequent ureterovaginal fistula. The fistula usually occurs a few centimeters from the bladder orifice; the fistula breaks through just about the time the constant drainage catheter is removed—from the ninth to the eleventh day after operation. In the previous report it was concluded that a ureterovaginal fistula meant ultimate nephrectomy but this has proved not to be true. There have been eight ureteral fistulas, or 12.3 per cent, in the 65 patients operated upon. One patient who had a huge tumor and who would never again be chosen for the Wertheim operation developed bilateral ureteral fistulas; she died six months after her operation. One patient is still leaking. In two cases it was necessary to do a nephrectomy, and in four the leakage ceased

TABLE I. COMPLICATIONS

	NUMBER OF CASES	PER CENT
Ureterovaginal fistulas	8	12.3
Ureterovaginal fistulas, healed	4	
Ureterovaginal fistulas, kidney removed	2	
Ureterovaginal fistula, leaking	1	
Ureterovaginal fistula, dead	1	

spontaneously. In three of these cases the kidneys are "dead," at least they do not function and no shadow is found after intravenous dye. No urine comes from the ureter at cystoscopy and catheterization of the ureter is not possible. In the one patient who is still leaking it is conceivable that the fistula might heal or that bowel or bladder anastomosis might be possible. So far, the Urologic Staff at Pondville Hospital has not been able to find sufficient ureter to anastomose to the bladder or to implant into the bowel. Of the four ureters that healed, one healed in two months, one in four months, one in six months, and one in nine months after leakage was discovered. It is therefore obvious that of the sixty-five patients only 6 per cent had the kidney removed or are still leaking. In the first series there were no vesicovaginal fistulas; one recent case may possibly fall into this category, but as it has not yet been proved, it is included here as a ureterovaginal fistula and will be until proved to the contrary. It is to be noted that in 15.3 per cent of all cases ureteral dilatation was present before operation and yet it was not in these patients that the ureteral fistulas occurred. It is hoped that with better knowledge of the blood supply of the ureter and with greater ability to free the ureter from its groove around the upper vagina and into the bladder, fewer fistulas will develop. If this problem can be overcome, surgery will prove more satisfactory than any form of radium or x-ray treatment for early cervical cancer.

Lymph Nodes

The fifth reason for performing the Wertheim operation, the lymph node problem, has borne out the findings of Bonney and Taussig to a surprising extent. Lymph nodes were involved in twelve patients: the iliac nodes in six, the obturator nodes in seven, and the ureteral nodes in one. More than one area was involved in two patients. Therefore, 18.4 per cent of these very early cases had lymph node extension and all of them, I believe, would have died if radium were the treatment of choice. Of this group of patients, three, or 25 per cent, of those with positive nodes are known to be dead. One case is lost and one has recurrent disease. It is evident, therefore, that of the group with nodes, 41.6 per cent should be considered as not cured. If any of these patients with nodes is salvaged, the operation is worth while, and it is probable, considering the length of time that has elapsed since operation, that some of the cases will live. One other patient had a metastasis to her Fallopian tube and she surely would not survive if radiation alone had been used.

TABLE II. LYMPH NODES

	NUMBER OF CASES	PER CENT
Positive nodes	12	18.4
Positive nodes, dead	3	25.0
Positive nodes, dead, lost, or recurrent	5	41.6
Positive nodes, living	7	58.4

It is my belief that better results can be obtained following surgery when the lymph nodes are involved than following radiation. In this series of cases, 18.4 per cent of 65 patients had positive nodes, and 58.4 per cent are known to be living and well.

X-ray and Radium Treatment

Twenty-four patients either had complete x-ray and radium treatment, or one-half of the complete x-ray and radium treatment. Of this group two patients, or 8.2 per cent of the twenty-four are dead; two patients, or 8.2 per cent, have a ureterovaginal fistula. There were 14.6 per cent of fistulas among the patients who had no previous radiation treatment. Radiation did not seem to be an etiological factor in the development of fistulas. Five patients who were radiated, or 20.8 per cent, had positive nodes, while there were 17 per cent with nodes who had no radiation. In this series patients treated with x-ray and radium had approximately the same number of involved nodes as those without radiation. The number of patients is too small to be convincing, yet there were about the same number of patients with involved nodes in both groups, fewer patients with fistulas in the radiated group, and as many patients died in both groups. No suggestion can be deduced from this study that radiation treatment before operation is or is not beneficial. From the technical surgical point of view, there is very little difference in the dissection during the operation.

TABLE III. RADIATION

	RADIATED CASES NO. PER CENT	NONRADIATED CASES NO. PER CENT
Total number	24	41
Nodes	5 (20.8)	7 (17.0)
Fistulas	2 (8.2)	6 (14.6)
Dead	2 (8.2)	2 (7.3)

The Groups and Grades of the Cancer

The cases were grouped according to the American College of Surgeons' classification. There were 45 patients in Group A, or those cases involving the cervix only; 15 were in Group B, or those involving the cervix and vagina; and 5 were found to have extension in the broad ligament and were placed in Group C. There were 6 adenocarcinomas and one adenoacanthoma; 8 cancers were called grade 1; 17, grade 2; 26, grade 3; two, grade 4; and in 5 no grade was reported.

Results

There was *no* postoperative mortality in this group of sixty-five patients. This result is of major importance, for with the excellent results obtained by radium and x-ray treatment, no one would dare do surgery if the mortality were high. These figures prove that surgery can be done safely, and because of that it is appropriate that a large series of surgical cases be tried. The fear of a high mortality should no longer be a deterrent to the surgical treatment of selected cases of cervical cancer. Of sixty-five patients, five, or 7.7 per cent, are known to be dead and three of these patients had positive lymph nodes. Of the fifty-three patients who did not have positive nodes, only two are dead, or a survival rate of 96.3 per cent. Of the total of sixty-five patients, there are five dead, two with recurrent disease, and one lost, or a total loss or probable loss of 12.3 per cent or a corrected survival figure of 87.7 per cent.

TABLE IV. RESULTS

Number of cases	65
Postoperative deaths	0
Dead	5 (7.7%)
Living with disease	2
Lost	1
Dead, living with disease, or lost	8 (12.3%)

It is not possible to compare these figures with known five-year results following radium, but of this group of patients, 2 are alive five years or less; 5, four years or less; 9, three years or less; 18, two years or less; and 25, one year or less. Undoubtedly some will die, but judging from the results and seeing the patients in follow-up clinics, the author predicts that the ultimate results of this five-year series will be more satisfactory than similar groups treated by radium or radium plus x-ray therapy.

No correlation could be made of the eight patients who died, were lost, or are living with disease as to the extent of the disease or grade of the cancer. The dead or dying are too few to attempt any statistical evidence. Three who died had positive lymph nodes, which is perhaps a significant fact.

Conclusions

1. Surgical removal of the early cervical cancer is as safe as radiation treatment.

2. The number of fistulas of the ureterovaginal type is too large, but with a better understanding of the blood supply fewer such calamities are expected.

3. Lymph node involvement is curable by surgery as evidenced by the reports of Bonney and Taussig, and the results of this series point toward that eventuality also.

4. It is the belief of the author that properly selected cases operated upon by the Wertheim-Clark technique and cared for by modern surgical preoperative and postoperative methods may improve the results in cervical cancer.

References

1. Bonney, Victor: AM. J. OBST. & GYNEC. 30: 815, 1935.
2. Lynch, Frank W.: AM. J. OBST. & GYNEC. 22: 550, 1931.
3. Idem: AM. J. Surg. 48: 249, 1940.
4. Meigs, Joe V.: Surg., Gynec. & Obst. 78: 195, 1944.
5. Taussig, Fred J.: AM. J. OBST. & GYNEC. 28: 650, 1934.
6. Idem: AM. J. Roentgenol. 34: 354, 1935.
7. Idem: AM. J. OBST. & GYNEC. 45: 733, 1943.

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Discussion

DR. VIRGIL S. COUNSELLER, ROCHESTER, MINN.—Carcinoma of the bladder is one of the most fatal lesions encountered. In this region the lesions are predominantly epithelial in origin, and in the cervix the same situation is true. I am stressing the behavior of epitheliomas in these various locations to emphasize the fatal consequences of this type of lesion. More and more, surgeons are advising total cystectomy with removal of all perivesical fat and associated lymph nodes, followed by extensive roentgen therapy in cases of infiltrating lesions of the bladder. One might ask what this has to do with carcinoma of the cervix. The two lesions are in very close proximity, the cellular structures are very similar, and the radical surgical treatment is not dissimilar. A few years ago, total cystectomy, seminal vesiculectomy, and prostatectomy carried a high mortality rate, but this is not so today. The same holds true for radical surgical treatment of operable carcinoma of the cervix.

For many years it has been considered by authorities that radium treatment or roentgen therapy plus radium therapy was the accepted treatment for carcinoma of the cervix. In fact, it still is and should be in a large percentage of such cases. But the lesions which should be treated by radium are not what Dr. Meigs is discussing. His thesis is limited to the operable group, and I am happy that I can agree with him that the radical removal of the lesion and dissection of the regional lymph nodes is the proper approach. Radical surgical mastectomy with complete dissection of the axillary lymph nodes is the accepted treatment for carcinoma of the breast. The same type of treatment should be employed in cases of high-grade epithelioma of the lip with involvement of the lymph nodes. I believe these are analogous to epithelial lesions of the cervix uteri.

I was especially interested in the first and second tables presented by Dr. Meigs. The first table dealt with ureteral fistula, the most important complication but by no means a fatal one. I believe the incidence which he reported is higher now than it will be in the future. I have been aware of the multiple blood supply of the lower part of the ureter for some time, but, in spite of extreme care, I have noted that the lower segment of the ureter sloughed in some cases in which the ureter was implanted into the bowel. When such a complication does occur, I believe it is best to do a nephrostomy to prevent hydronephrosis and repeated infection, as a safety method, and to await developments. I have records of patients who have lived twenty years after bilateral nephrostomy and are in otherwise good health. It must be emphasized that the position at which the ureter enters the bladder is the most fixed portion of the entire ureter and that its blood supply can easily be injured. Furthermore, there are anomalous vessels to the ureter in this location just as there are frequently at the ureteropelvic juncture.

Involvement of lymph nodes in cases of malignant lesions is a good index as to the possible extent of the lesion and the grade of malignancy. It gives considerable criteria on which to base prognosis. It is of interest, therefore, that in 18.4 per cent of this series of sixty-five selected cases of carcinoma of the cervix, the lymph nodes were involved. Gratifying indeed is the fact that 58.4 per cent of the patients are living. I am quite sure that it is impossible to cure patients with this disease by radium or roentgen therapy or any combination of both if the lymph nodes are involved.

Dr. Masson, my surgical colleague, has been interested in the Wertheim hysterectomy for many years. In looking over our records during the last thirteen years, Dr. Masson, Dr. Waugh, and I found that we have done a Wertheim hysterectomy in 113 cases. In this group, there were three urinary fistulas. There were two deaths from pulmonary embolism, one from peritonitis, and four from bronchopneumonia. During the past year we did this operation in sixteen cases with one death and no fistulas. In an institution such as the Mayo Clinic, I believe these lesions are seen at a slightly later stage perhaps than in private practice. I say this because in 80 per cent of the cases of carcinoma of the cervix the lesion is considered inoperable on account of the extent of the lesion alone, when the patients first are seen at the clinic.

In closing, I want to stress the importance of Dr. Meigs' contribution, and I believe the percentage of cases in which surgical treatment is applicable will remain around 20 or less, unless it is possible to examine the patients in an early stage of the disease.

DR. A. N. CREADICK, NEW HAVEN, CONN.—Dr. Meigs' first contribution is the description of the blood supply to the ureter. His second contribution is the observation that the obturator glands are so frequently involved, which explains why so many of our recurrences have obturator pains which we could not explain until we later felt the masses in the pelvis. But far more important to the subject of the cure of cancer is that Dr. Meigs has had the temerity to remove the site of the growth. The Connecticut Division of the American Cancer Society spends \$10,000 a year in propaganda advocating cancer-awareness, early diagnosis, and semiannual physical examinations. We are faced with a defeatist attitude on the part of the profession itself. The expert medical men, whether they are radiologists or surgeons, are unhappy over their statistics and the limitations of their accomplishments. The average practitioner is defeated because he sees only the neglected and incurable cases which he must attend through the prolonged incapacity and slow exitus. One said to me lately, "Why should I look for cancer? What would I do with it if I found it?"

A great deal of money is being spent on cancer research, and some day a chemical solution may be found. But until that day we have no program except to encourage (a) early diagnosis, an alert medical profession, and a cancer-conscious laity; (b) early total and radical extirpation of the disease; and (c) eternal watchfulness thereafter that the same or a new growth shall not occur.

In the face of these facts I turn to Dr. Katherine MacFarlane's contribution of last June. You remember she stated that 1,876 women had reported for semiannual physical examinations and three carcinomas of the cervix were discovered. They were treated and are still alive. Now there have been established five cancer-prevention clinics in Philadelphia and we will watch their development with interest.

We are beginning a cancer-prevention clinic in New Haven, at first in the postpartum clinics, then among our hospital employees, then among the big employers of women. We hope to stimulate similar clinics in Hartford. I know of no other way than this to discover cases early enough for such a procedure as that we have seen this morning.

DR. WILLIAM H. VOGT, St. Louis, Mo.—This is a serious operation and, as Dr. Meigs has brought out, it takes a great deal of technical skill and a great deal of experience. The operation cannot be learned by observation; it cannot be learned by mere assisting, but it must be learned on the cadaver. To dissect out the glands, and the ureters, and to remove a large portion of the parametrium and the vagina is an extensive procedure and can be followed by many complications.

The gynecologic profession for many years has been radium-conscious and the results with radium, as brought out here this morning, have not been entirely satisfactory. The general surgeon removes carcinoma from any place in the body, from the scalp to the palmar surfaces of the feet when he can, and I could never understand why the uterus should be eliminated from that method of procedure. The surgeon today gets results with radical amputation of the breast—why not with radical operation for carcinoma of the cervix? One reason is, I think, that the operation which is called the Wertheim operation is in too many instances not the Wertheim operation. It is often a makeshift and not the operation originally designed for the cure of that disease.

I talked before a county medical society one time and one man in the discussion, a rather keen observer who had been in the practice of medicine a good many years, said he had watched the change in the treatment of carcinoma of the cervix. He observed that prominent men who had in former years advocated surgery for this condition had gone over to radium. I had described this operation as a serious and difficult one in which a large portion of the broad ligaments and the vagina were removed and the uterine arteries tied off at their origin and I described the difficulties that might be encountered. He said, "I wonder whether these men who formerly did that operation and have now gone over to radium feel that they are no longer physically able to carry out that procedure?" It was not a bad observation, for it takes not less than an hour and fifty minutes and sometimes two and a half hours to do this operation and is certainly no easy task for the surgeon.

Dr. Meigs has brought out one important thing in the matter of ureteral fistulas. I am satisfied that injury to the ureters can in most instances be satisfactorily avoided. The reason fistulas develop is chiefly due to interference with the blood supply of the ureters. If the blood supply is not too greatly interfered with, the incidence of fistula following this operation will be greatly diminished.

DR. THADDEUS L. MONTGOMERY, PHILADELPHIA, PA.—From the outset I would say that Dr. Meigs' operation is the most complete eradication of carcinoma of the cervix, and of carcinomatous glands of the pelvis, which I have ever seen performed or described in the literature. It will be most interesting to compare the ultimate results of this method of therapy with the many series of cases treated by radium and x-ray.

Dr. Meigs mentioned that in several of his cases, preliminary x-ray therapy was employed. I would like to know whether he found any appreciable effect of such treatment upon the primary growth and the lymphatics. Theoretically it would seem a good procedure to perform preliminary x-ray therapy in all of these cases whether the cervical carcinoma is to be ultimately treated by radium or by surgical extirpation. While one does not anticipate a cure with the preliminary x-ray therapy, the amount of regression in the primary tumor is oftentimes amazing. We have found this method of treatment particularly efficacious, for instance, in carcinoma of the body of the uterus.

As to the work of Dr. MacFarlane, and the effect it has had on the education of the laity and stimulation of the profession, there is little or no question. Dr. MacFarlane's clinic has done more to arouse the interest of the laity in semiannual health examinations and to stimulate the profession to provide regular gynecologic checkups, than any other single event in the history of Philadelphia medicine. I find in my own gynecologic practice that almost one-third of the office work today

is the performing of semiannual gynecologic check-ups. This is a tedious task and takes a considerable portion of the office hours. Nevertheless, I feel it is the greatest service which we gynecologists can perform in preventive medicine and early diagnosis and cure of gynecologic carcinoma.

DR. HERBERT E. SCHMITZ, CHICAGO, ILL.—I think that some of us have lost sight of the original intent of Dr. Meigs' work. He is not attempting to pit surgery against radium therapy, as have some of our discussants. If surgery had proved to be the only correct treatment of carcinoma of the cervix, radiation therapy could never have gotten a foothold. Gynecologists were looking for a treatment more safely executed and more satisfactory than the radical operation.

Radium and x-ray will in no way interfere with those cases that are best treated with surgery. We have demonstrated that radiation does not increase operative difficulty, and that is something to be remembered. I have observed surgeons operating in a field which was invaded by carcinoma which increased the bleeding and the difficulty of dissection, and interpreting that effect as due to previous radiation.

Surgery should be limited to those cases where the tumor is operable and in young individuals who can stand the operation. There still remains that group of cases advanced beyond surgery where radiation has to be employed. As yet, I have not seen surgical statistics showing a survival rate above that of irradiation therapy in a comparable group of cases.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—Cancer is now a permanent term for all types of malignant growths in all kinds of tissues. It is uncontrolled growth of one or more cells, or tissues of the body.

1. Cancer consists of biologically incomplete, and perverted tissue cells derived from immaturesly completed cells within a local area of body tissue. Histologically cancer cells persistently maintain abnormalities of form. Their functions are inconsistent with continuance of life by the body host.

2. The cause of cancer is always an irritant of sufficient potency to alter permanently cellular growth behavior, and cell differentiation into specific tissue patterns. Example of such irritants are called carcinogens, e.g., *radium* feedings have produced sarcomas; *carbon tetrachloride* has produced hepatomas; *wheat germ oil* may malignantly irritate generative tissues; *benzpyrene* is a potent agent for producing cancer in mice.

Long-continued physical irritants contacting cuticular, mucocutaneous, and cutaneous tissues result frequently in epidermoid carcinomas. Reductions and obliterations of adrenal or pituitary tissues directly or indirectly predispose to cancer occurrences.

Reduction of tissue calcium alters resistance to cancer. Genetic deficiencies predispose tissues to cancer.

Resistance to prostatic cancer is produced by stilbestrol, estrogen, progesterone. Removal of testes may depress cancer growth in prostatic tissue. Removal of the thymus and of the ovaries in experimental animals may have profound influence upon cancer development.

3. In prevention of cancer, efforts succeed in different ways. (1) By restoring displacements of tissues especially at marginal positions. (2) Removal of inflammatory or other constant irritants. (3) Adjusting long-continued chemical, and hormonal imbalances by restoring the surrounding growth stimulating connective tissue substance to normal. (4) Breeding control. Stockbreeders cull out and breed out defective animals. (5) Removal of cancer tissue while it is localized and not in the invasive stage by surgery, x-rays and radium; 36,000 cancer cases reported

A MORTALITY STUDY OF 187 DEATHS IN 66,376 LIVE BIRTHS*†

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(From the Margaret Hague Maternity Hospital)

WHEN one sees the excellence and completeness of the many studies on maternal mortality which have appeared in our literature, one should approach the presentation of another review of a similar nature with no small degree of compunction. However, we are of the opinion that the material here analyzed has some aspects which are peculiar to it and which are thought to be of sufficient interest and importance to warrant further exploration and presentation.

We are offering a study of the maternal mortality in the Margaret Hague Maternity Hospital, Jersey City, New Jersey, from the opening of the hospital in October, 1931, through 1943. During this period, there were 66,376 live births at the hospital, with 187 maternal deaths, a maternal mortality rate of 2.8 per 1,000 live births. No attempt at correction of any kind has been made; any patient pregnant or recently pregnant (i.e. who was readmitted to the hospital post partum), who died in the hospital, whether delivered outside or readmitted post partum, has been included, the only exception being the exclusion of two cases of criminal infected abortion.

A breakdown of the 187 deaths for purposes of presentation will be made into two main groups. In the first will be considered 143 cases which fall into groups quite directly related to pregnancy.

TABLE I. SUMMARY OF MORTALITIES

	PREVENTABLE	NONPREVENTABLE
Puerperal infection	19	23
Eclampsia	7	14
Other toxemias	-	18
Hemorrhage	7	11
Rheumatic heart disease	5	9
Rupture of uterus	9	2
Emboli, sudden death	2	9
Anesthesia	2	6
Pneumonia		12
Tuberculosis		8
All other causes	4	20
	55	132

Forty-two deaths were due to infection, 21 to eclampsia, 18 to other toxemias, 18 to hemorrhage, 14 to rheumatic heart disease, 11 to rupture of the uterus, 11 to emboli or "sudden death, and 8 to anesthesia.

Each of these various groups will be studied further, but for purposes of definition, permit me here to state that by infection we mean any one of the various clinical or pathologic manifestations of the disease.

*Read at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., September 7, 8, and 9, 1944.

†Owing to lack of space it was found impossible to include here the extended detailed tabulations which accompanied this article.

The term "other toxemias" is used to designate that large group of cases which loosely hang together as chronic nephritis, hypertensive disease, and cardiovascular renal disease; in short, those cases not classified as eclampsia or acute or specific toxemia. It was impossible to reclassify them under the more recent classification promulgated by the American Committee on Maternal Welfare.

By sudden death we mean some few cases where it was impossible accurately to fix an anatomic or pathologic cause and in most of whom an embolic phenomenon was thought to be the most likely etiological factor.

The classification of clinic, nonclinic, and private patient occurs repeatedly throughout. By clinic case is meant that class of patient who is registered in our Antenatal Clinic and for whose care the attending staff of the hospital is wholly responsible. By nonclinic is meant the patient who never registered in the Clinic and comes to the hospital, generally as an "emergency case." Finally, by private case is meant the patient for whose care some private physician is wholly responsible prior to admission. Patients in this group have their problems handled by their own private doctors and occasionally are admitted to the hospital with complications which have been treated for some time at home, often enough inadequately. Their care while in the hospital, of course, is subject to compulsory consultative advice by the attending staff for any complications or operative delivery. This makes it possible for us here to draw some comparisons between the three afore-mentioned types of services.

In the second main subdivision, we present forty-four cases, most of them of a rather miscellaneous nature, and a further review will be made of them.

Returning now to the forty-two cases of puerperal infection, they will be presented from the viewpoint of the type of delivery.

Puerperal Infection

Our approach to the problem of puerperal infection in this review has been that unless a definitely known and proved endogenous source of the infection existed, or unless we could establish an exogenous source in no way associated with hospital management or personnel, then the onus for the infection was placed on us and the death was deemed preventable. I know full well that this will result in our assuming responsibility for some cases in which de facto we have no real responsibility, but as I see it, unless this is the attitude adopted, corrections and excuses could be made and any good that might accrue from this or similar studies would be vitiated.

Of the thirteen cases of puerperal infection with normal spontaneous delivery, four were probably preventable and the source of infection was undoubtedly due to the obstetric management. In two cases there were baggings (one of these had a long labor), and in a third case, an operative interference, the draining of a pelvic abscess, was undertaken on the forty-fifth postpartum day, during the course of a prolonged clinical puerperal infection. Perhaps this was an operative procedure injudiciously undertaken. The fourth case, again one of operative interference, had a reconstruction of an old laceration of the sphincter ani after the completion of the third stage of labor. This too was prob-

ably a case of unwarranted surgical manipulation. Four of the remaining nine cases were quite definitely nonpreventable. One came to us as a transfer from the Contagious Disease Hospital with erysipelas. Another, during the course of sulfonamide therapy, had a hypoplasia of the bone marrow. A third developed a generalized septicemia from a hemolytic streptococcus finger infection. The fourth had an antepartum chill with a rise in temperature and a rapid downward clinical course of puerperal infection with acute yellow atrophy of the liver, proved at autopsy.

We now come to the consideration of the four fatal cases of peritonitis. The exact source of the infection could not be determined or even remotely approximated. After a two-hour labor with no vaginal examinations and one rectal examination, one patient expired on her sixth postpartum day. Another, after a three-hour labor, with no vaginal examination and with but one rectal examination, expired on the fifth postpartum day, and the third was delivered one hour after her admission to the hospital with no vaginal examination, one rectal examination, and expired on her fifteenth postpartum day. The fourth and final case in this group had a four-hour labor, no vaginal examination, one rectal examination, and in twenty-four hours her temperature began rising and remained up, and she expired on her forty-third postpartum day. No specific organisms were ever isolated.

A close scrutiny of the records of these four cases indicate no reason of any kind for the subsequent infected course. The possible role played by an endogenous focus was assessed and both aerobic and anaerobic bacterial studies were made, but were not sufficiently conclusive. These cases and cases of a similar nature offer a real challenge in the further study of the preventability of puerperal infection. From this analysis we are unable to offer much.

There was one case which could be attributed to the patient's neglect in not seeking earlier hospitalization. This was an individual who remained at home three days with ruptured membranes, two and a half hours after admission to the hospital delivered a stillborn macerated fetus, and she herself expired in less than twenty-four hours due to gas bacillus infection.

In recapitulation, therefore, it may be said that of the thirteen fatal cases of puerperal infection occurring after normal spontaneous delivery, four were probably preventable in the sense that some operative interference was undertaken which might in each case explain the subsequent untoward outcome.

There were eleven cesarean section deaths due to puerperal infection. The indication for the section was, in all cases but two, cephalopelvic disproportion. In these two cases, the indications were (1) transverse presentation, and (2) an abruption of the placenta occurring during the course of hypertensive cardiovascular renal disease. There were four low transverse cesarean sections; two classical, one of these a low classical in a case of abruption, and one a modification of the Beck technique; and four extraperitoneal sections, two following the Latzko technique, and two the supravescical technique. If one approaches the problem of fatal puerperal infection occurring after cesarean section as a distinctly preventable entity unless some very definite and unquestionable focus other than the operative undertaking can be determined, then of the eleven cases, ten are to be considered preventable. The case of abruption is alone excepted.

No detailed study or comment is possible concerning the seven cases delivered at home. We have no way of determining the intrapartum care or the postpartum care of any of these patients, and we do not in our own figures hold ourselves accountable for their unfavorable course. For the purpose of study of our experience, all seven are considered nonpreventable.

Of our total of puerperal infection deaths, five cases were delivered by forceps operation. There was nothing of any unusual moment in the past history of any of these to explain the subsequent course. Two had antepartum morbidity or intrapartum morbidity, and one was in labor for eighty-two hours. As was indicated in the comment above concerning puerperal infection following cesarean section, since there was no other ascribable focus for any of these infected courses, we accept all five as preventable.

Of the remaining six cases of puerperal infection, the three postpartum readmissions, the two spontaneous abortions, and the one peritonitis following appendicectomy, all are considered nonpreventable from the hospital standpoint.

Eclampsia

Out of a total of 21 deaths due to eclampsia, 4 were clinic, 10 were nonclinic, and 7 were private patients. There will undoubtedly be a discrepancy between the number of fatal eclampsias reported here and the number reported by our Biochemistry Department because I have included two cases which the pathologist has labeled eclampsia but with which classification the Biochemistry Department is not in full accord.

Two of our clinic cases were probably preventable. In one, the clinic overlooked some early signs, and in another, we waited too long in dealing with the pre-eclampsia. The other two cases are considered nonpreventable, one having come in with some bleeding, and a post-mortem examination indicating some liver necrosis. The other was kept at home for a long time because she was thought to be having epileptic seizures. Of the 10 nonclinic cases, as one would imagine, by far the vast majority, 9 of the 10, are considered preventable, 3 because the physician in charge either failed to recognize or failed to treat energetically enough the very evident and patent signs of severe pre-eclampsia. There were 7 private cases of fatal eclampsia, and of these, 4, after a review of the case records, would be considered preventable, and 3 nonpreventable. Of the entire group of 21 cases, 10 were admitted in coma, 8 expired undelivered (one clinic case epilepsy? 3 nonclinic, and 4 private cases).

The four clinic cases in this series, against ten nonclinic and seven private cases, tend to emphasize that the management and care given the clinic cases of pre-eclampsia is very likely to avert eclampsia in most instances. Admission to the hospital at the earliest possible time to treat the pre-eclampsia adequately is the only method from which one may expect the desired results. This means close and prolonged supervision and hospitalization for as long a period of time as is deemed necessary. This leaves us with a quite definite element of preventability in 15 of a total of 21 cases.

Other Toxemias

Because of the very great difficulty encountered in breaking down these groups into hypertensive disease and renal disease, it was thought best to present all deaths in the toxemic group (other than those due to eclampsia) as a unit. The data necessary accurately to establish the

differential diagnosis between the various subdivisions of this group was in the main either lacking or not sufficiently set down.

This group includes only those cases who began the pregnancy under examination with incontrovertible evidence of previous disease of the cardiovascular renal system. In the main, therefore, we inherit in this group a poor type of risk whose life expectancy at best is curtailed, and for whom not much can be done at this time. We, therefore, feel that we are justified in saying that there is very little that the obstetrician can do to prevent the fatality once the basic fundamental cardiovascular renal pathology is well established and the period of gestation far advanced.

These patients without exception evidenced the clinical course of severe hypertensive cardiovascular renal disease as seen in the adult male or adult nonpregnant female, and by the time we saw them, they were well beyond the reach of therapeutic good. The terminal issue, therefore, is regarded as a nonpreventable maternal death as viewed from the obstetrician's standpoint.

There were thirteen postmortem examinations in this group of eighteen, and the findings all included varying degrees of arteriosclerosis, nephrosclerosis, malignant nephrosclerosis, chronic nephritis, cardiac hypertrophy, and dilatation. There were two cerebral hemorrhages.

Hemorrhage

There were 18 deaths due to hemorrhage: 8 postpartum hemorrhages; 5 abruptions; 2 postoperatives; 2 placenta previas; and one intraperitoneal hemorrhage.

In attempting to evaluate the problem of preventability in a group of postpartum hemorrhages, certain very real difficulties present themselves.

Granted a patient with no untoward past history and a normal pregnancy with a not too long labor and either a normal spontaneous delivery or a relatively easy forceps operation, who immediately, or some few hours postpartum, begins bleeding briskly from the vulva—oxytocics, transfusions, plus other supplemental fluids are used. Inspection and examination of the birth canal for lacerations is made, and as indicated, if need be, a hysterectomy is performed in order to control a hemorrhage which bids fair to go on and terminate fatally. In spite of all this and the widespread use of all the other available instruments of aid at the disposal of the attendant in a well-equipped and completely manned institution, death ensues.

Is a death of this nature preventable or nonpreventable? We feel that in the absence of errors in clinical judgment, such deaths under the circumstances set forth are nonpreventable.

Accepting these fundamentals as criteria, five of these cases are considered nonpreventable.

Placenta Previa.—Of the two cases of placenta previa, one case is deemed preventable, and the other nonpreventable.

Abruption.—When one comes to discussing complete abruption of the placenta, he is face to face with probably the most catastrophic clinical entity in the entire field of obstetrics. When one attempts to discuss the element of preventability in this group, many hazards present themselves; one must examine carefully whether or not the underlying toxemia (if one was present) was treated adequately; whether or not the proper selection was made as to time and type of delivery and anesthesia;

and finally, whether all provisions were made properly and energetically to handle the hemorrhage, the accompanying shock, and the postpartum complications present. With this in mind, we feel that four of these five cases were not preventable, the only exception being a patient with a nephritic toxemia who was in the hospital for three weeks and was being "carried along" when she abruptly her placenta.

The question of whether cesarean section or delivery through the birth canal is the better suited, we cannot prove from these five cases. However, three of them at postmortem examination had considerable hemorrhage into the peritoneal cavity, into the uterus, and extending out into the broad ligaments.

The discovery of such a pathologic state is possible only if one elects to do a cesarean section. The possibility of this complication has in many instances determined our choice in method of delivery.

Postoperative Hemorrhages.—There were two postoperative deaths from hemorrhage following cesarean section, and in one there was an error in operative technique. A 40-year-old gravida iv with rheumatic heart disease had an elective cesarean section with tubal sterilization and expired twelve hours after operation. At postmortem examination, there was found an extensive hemoperitoneum.

The second patient died during the operation due to an error in judgment, in that the exact amount of bleeding was not properly assessed at the time of operation, by the operator. She was a 35-year-old primigravida who, during the course of a Latzko cesarean section, expired on the table from hemorrhage.

There was one death from intraperitoneal hemorrhage which is deemed nonpreventable, a 30-year-old gravida iv, a private patient, admitted to the hospital in shock and not in labor. Immediate abdominal operation revealed a bleeding splenic vessel, and she expired within a matter of hours. At autopsy, acute hemorrhagic pancreatitis with necrosis throughout the pancreas, and massive necrosis of the pancreas with erosion of splenic vessel was disclosed.

Rheumatic Heart Disease

There were fourteen deaths from rheumatic heart disease. Seven of these were clinic cases, and of these, in only two was the outcome thought to be preventable. In one of these, a hysterotomy was undertaken before the patient had fully recovered stability of her cardiovascular tonus, and in the other, the patient was discharged from the hospital (contrary to our principles of management) by a new cardiologist who was substituting for our attending cardiologist who is on active military duty. In two other clinic cases, both patients refused to cooperate and abide by the instructions and advice given them, and the responsibility for the failure is definitely theirs. The remaining three were nonpreventable.

There were four private patients in this group, and in only one case was the problem thought to be nonpreventable. There were three non-clinic cases and, in two cases, another hospital is responsible, having in both instances, admitted the patient in failure and then discharged her with her status improved; in neither case was the patient given any instructions as to further care or advised to register in the Antepartum Clinic of this hospital. The third nonclinic patient refused to register in the Antepartum Clinic because she feared she would be hospitalized for her present signs of failure as she had been in her previous pregnancy for fourteen weeks.

This leaves us with a total of fourteen cases of rheumatic heart disease with the element of preventability present in only two cases as far as the hospital is concerned, and in three cases as far as it relates to the private physician.

Now our criteria of adequate care for the pregnant cardiac necessitates the making available to patients of this type, at the earliest signs of decompensation, facilities for prolonged periods of complete antepartum bed rest, running in some cases for as long as six months. It is our definite feeling that only by this method can one decrease the incidence of failure and eventually death in rheumatic heart disease complicating pregnancy.

If this period of prolonged bed rest for the patient with rheumatic heart disease complicating pregnancy proves to be a severe economic problem for either the patient or the hospital caring for these patients, then perhaps the time is near at hand when what is considered the basic needs of these patients might well prove to be more of a socioeconomic problem than one of medical management.

Two of these patients were delivered at home and admitted to us post partum in advanced failure. Five died undelivered. Of this total of 14 cases, 9 were admitted in advanced failure. One died 3½ hours after admission, the others 19 hours, 15 hours, 12 hours, 16 hours, 3 hours, 11 hours, 8 hours, 21½ hours, all of which definitely emphasizes the tremendous gravity of the problem of advanced heart failure in rheumatic heart disease complicating pregnancy.

Rupture of Uterus

There are 11 cases of rupture of the uterus, varying in age from 26 to 40 years; 10 multigravidas and one primigravida; 10 white patients and one Negro. Five of the 11 were clinic patients, 4 were private patients, and 2 were nonclinic patients. The past medical and obstetric histories were not of any particular significance in any case, except that on the whole they all had large babies during their previous pregnancies. Two of the 11 had transverse presentations intrapartum, one of them with a prolapsed cord. The most significant factor in the whole analysis is that 6 of the 11 had podalic versions with breech extractions. Two others went into shock during labor and had the clinical picture of a rupture of the lower uterine segment as seen in obstructive labor after development of a Bandl's ring. Seven of the 11 had hysterectomy performed, 2 others had repair of the lacerated cervix, and 2 were never in clinical condition to warrant operative interference of any kind. All 11 resulted in stillbirths. The site of the tear was in the lower uterine segment from an extension of a cervical tear in 8 of the patients, and in 2 in the lower uterine segment at the site of reflexion of the peritoneum from the bladder into the uterus, and one on the posterior surface of the lower uterine segment.

The one factor that stands out most prominently is that version in a multipara with previous lacerations of the cervix may result, and often does result, in extension of the previous cervical tear up into the lower uterine segment, with fatal consequence. It happened in 6 of the 11 cases here presented.

The active clinical management of many of these patients was in the care of the House Staff during their labor, and repeated errors have occurred in management. The most frequent clinical mistake was that an emergency was deemed to be present which necessitated the im-

mediate undertaking of a version. This version, as has already been indicated, not infrequently resulted in an extension of a previous cervical tear. From a standpoint of preventability, one must say that probably 9 of these 11 cases could have been prevented had they been differently managed. In one, the patient expired in the admitting room within a matter of minutes after she came into the hospital. And in another, a patient with hypertensive cardiovascular renal disease had a convulsion in the admitting room and died in one hour. At autopsy, the cervical tear was discovered.

Embolus and Sudden Death

There are 7 cases of embolus resulting in death: 3 following normal spontaneous delivery, 2 following low transverse cervical cesarean section, 1 forceps, and one patient was undelivered. The antepartum complications were interesting and, in some cases, were sufficient to explain the subsequent course of events. One patient had attacks of ventricular tachycardia of a disabling nature throughout her pregnancy. Two had pre-eclampsia, and one of these had a complete abruption of the placenta. Another patient was admitted with paralysis of the right arm and other very definite clinical evidence of cerebral injury. The two patients with pre-eclampsia can probably be classified as preventable, inasmuch as the acute toxemia could probably have been prevented to some degree by earlier management. These two cases are the only ones in the entire group of seven which, upon careful analysis, any amount of preventability is present.

In all remaining cases in this group called "sudden death" for purposes of this presentation, no definite or reasonably definite known cause could be found for the exitus.

History No. 33889, 27 years old, para ii, gravida iii, white, a nonclinic patient, admitted eleven weeks pregnant with spotting of only moderate amount, was found dead in bed eight hours after admission to the hospital. No autopsy.

History No. 30640, 24 years old, gravida i, para i, white, a nonclinic patient was admitted to the hospital with a history of an incomplete spontaneous abortion and residual erysipelas of the face. Temperature 99.2° F.; pulse 96; respirations 26. Patient was found dead in bed twenty-four hours after admission to the hospital. No autopsy.

History No. 20014, 34 years old, para vi, gravida vii, white, a non-clinic patient, was admitted to the hospital with a diagnosis of avitaminosis and was found by the house doctor on rounds, cyanotic, pulseless, no respirations, and with half a breech delivered. Delivery was completed by birth of twins, both premature, and patient expired almost immediately, seventeen hours after admission to the hospital. No autopsy.

History No. 50296, 34 years old, para i, gravida iii, was sent into the hospital by a private doctor in state of terminal pulmonary edema with no known cause for the failure and expired in seventeen minutes. No autopsy.

There is nothing that we feel could be done to prevent the issue in the first three cases of this group. What might have been accomplished in the last case is an open question. So, it is reasonable to say that only two cases, and probably a third one, of the eleven in this group could have been prevented. The two cases emphasize the need for adequate antepartum supervision.

Anesthesia

There is a total of eight cases in which the anesthesia was the cause of death. There was nothing of any particular or outstanding significance as far as age, parity, past medical or surgical or obstetric history is concerned. Only one patient was a private case.

In two of these eight cases, open drop ether was the method of anesthesia, and in one it was used for sixty-five minutes, using a $2\frac{1}{4}$ pound can—perhaps too long and too much anesthesia. In the other, food regurgitated and asphyxiation occurred. This untoward result could not have been prevented because it is necessary often to anesthetize obstetric patients without much previous preparation of their gastrointestinal tract. In the other case, gas oxygen ether with chloroform added was used. This undoubtedly is a poor combination and should not have been used. Whether this fatality would have occurred without the addition of chloroform, is difficult to say.

There were five deaths in which spinal anesthesia was used. In one, a combination of 10 mg. of pontocaine and 100 mg. of novocain was used. In all others, 100 mg. of novocain was used. In two cases, the exitus was so sudden that the patient expired undelivered, and in the other case, an agonal cesarean section resulted in delivery of a living child. There will ever remain some risk due to anesthesia, and in a total of 66,376 births, 8 cases died of anesthesia, a ratio of 1 to 8,297.

This represents the sum total of our experience with anesthesia, and in attempting to assess the element of preventability, one must say that, with the exceptions noted, all the approved and standard technical criteria and procedures were followed and adhered to, and in viewing the problem from this standpoint, there is present an element of preventability in but two of the eight cases.

Pneumonia

There were twelve cases of pneumonia. In most cases, the patient was admitted with a far-advanced lobar pneumonia and expired sometimes within hours of the time of her admission. Four died undelivered. There was one postmortem and one antemortem cesarean section. One was a postpartum admission, and one a transfer from another hospital. There were only two living babies out of this group. A very interesting factor stands out quite prominently and that is that since 1936 there has not been a death at the hospital with pneumonia as the primary cause of death. The relationship between this date and the advent of the sulfonamide drugs is, to say the least, permissible of some interesting speculation.

All twelve deaths are regarded as nonpreventable.

Tuberculosis

In discussing our deaths from tuberculosis, it is evident from the sheets that seven of these deaths are transfers from the Hudson County Tuberculosis Hospital. These patients have their entire antepartum hospital care in the Tuberculosis Hospital and are sent to us only for delivery. They are therefore all nonclinic cases, and are all considered as nonpreventable obstetric deaths. The one patient not transferred from the Tuberculosis Hospital was a 21-year-old gravida i who was admitted to the Margaret Hague Maternity Hospital in labor and with what was thought to be an acute upper respiratory infection. She was delivered

by Kielland forceps after a sixty-two-hour labor. On her first postpartum day she had a temperature which was diagnosed as due to bronchopneumonia, and while running a febrile postpartum course, on her fifteenth postpartum day, she had a massive pulmonary hemorrhage and died. Postmortem report was chronic pulmonary tuberculosis with hemorrhage of the entire bronchial tree with asphyxiation.

Miscellaneous

There were 24 cases in this group and, as you see, on the accompanying chart there is quite a variety of diagnoses. Of the entire group, 8 were nonclinic patients, 10 were clinic patients, and 6 were private cases. Four cases expired undelivered. Four cases of this entire group are considered preventable, one of inversion of the uterus, and three of intestinal obstruction. The inversion of the uterus was a 31-year-old gravida ii who, after a 12½-hour labor, was delivered of a living child by elective low forceps. Thirty minutes following delivery, the patient went into shock and never responded to treatment. At postmortem examination, an inversion of the uterus was found with chronic healed endocarditis, mitral stenosis, and aortic stenosis.

There were three cases of intestinal obstructions. A 31-year-old gravida iv was admitted to the hospital and was thought to be in labor. It later developed that she had an intestinal obstruction of a mechanical nature, probably due to adhesions from a previous operation. She was not deemed a fit candidate for surgery.

A second patient, a 28-year-old gravida ii, was thought to have an obstruction with negative x-ray findings. She was operated on and the obstruction was found, but she failed to recover.

The third case, a 28-year-old gravida ii, developed some abdominal distention with some polyhydramnios. Her labor was induced and she delivered a small baby spontaneously. The abdominal distention now marked with considerable pain prompted surgical intervention. She died on the third postpartum day.

Cesarean Section Mortality for 1931 to 1943—All Causes

There were 23 cesarean section deaths: 15 clinic patients, 8 private patients; 19 white and 4 Negro. There were 6 extraperitoneal cesarean sections, 3 Latzkos, and 3 supravescicals.

Spinal anesthesia alone was used in 13 of these 23 cases, and in 3 spinal plus ether; ether alone in 2; gas-oxygen-ether in 2; local plus ether in one; cyclopropane in one; gas-oxygen with vinyl ether in one.

Causes of Death.—In 11 of these 23 cases, infection was the cause of death; in 3 hemorrhage; in 3 anesthesia, 1 ether and 2 spinal; in 2 emboli; in 1 heart disease; in 1 uremia; in 2 tuberculosis. The cesarean section in five cases was undertaken for purposes of sterilization: The first patient had rheumatic heart disease and died of postoperative hemorrhage. The second had a bad obstetric history, and died of infection. The third had rheumatic heart disease of which she died. The fourth had active pulmonary tuberculosis of which she died. The fifth had arrested pulmonary tuberculosis and died of a herniation of the gut through the foramen of Winslow.

Conclusions

One hundred eighty-seven maternal deaths are presented from a maternity hospital having three paralleling services: one a clinic service

which has, in close cooperation, antepartum, intrapartum, and postpartum services under the supervision of appointed obstetricians; the second, a nonclinic service offering hospital facilities for the emergent and oftentimes "in extremis" type of patient; and the third, a private service to which any ethical physician in the county may send his private patients.

Fifty-five of these 187 deaths occurring in 66,276 live births have sufficient clinical aspects to warrant them being labeled preventable as far as the hospital management of the case is concerned, a ratio of 0.82 per 1,000 live births.

No attempt is made to correct these 55, or to differentiate the non-clinic (emergency) or private cases from the clinic patient for which the hospital is fully responsible.

No correction is made for postpartum readmissions.

No correction is made for home deliveries (except against puerperal infection).

No correction against the transfer of patients from other hospitals.

The "other toxemias" group presents a very difficult problem in assessing preventability in maternal mortality. What good might come from prevention of pregnancy in this group we are unable to say. Our experience in dealing with it in reasonably far-advanced pregnancy was very unsatisfactory.

The greatest element of preventability in the entire group is in rupture of the uterus, hemorrhage, puerperal infection, eclampsia, and heart disease.

Rupture of the uterus, puerperal infection, and hemorrhage can be combated only by increased clinical vigilance and further improvements in general and special technique.

Some hope for a further reduction in rheumatic heart disease and eclampsia groups is anticipated by earlier and longer periods of antepartum bed rest.

Discussion

DR. WILLIAM R. BARNEY, CLEVELAND, OHIO.—Reviewing the deaths in approximately 40,000 cases at Cleveland Maternity Hospital, eclamptic cases have the greatest mortality rate, there being a 15 per cent death rate in all cases. No great disparity is present in clinic or private case, although the clinic cases are three times more frequent (45 to 15).

Since Bryant and Fleming reported the results in 120 cases of eclampsia treated with *Veratrum viride* with only two deaths, both resulting from infection on the twelfth and sixty-fifth day post partum, we have been prone to use their technique.

The rationale in using *Veratrum viride* is the general vasodilation which ensues, thus overcoming the vasoconstriction. In addition, the fall in blood pressure relieves an overburdened myocardium and prevents cerebral accidents, common causes of death. Additional therapy of intravenous glucose and magnesium sulfate (10 c.c. of 50 per cent solution), every 12 hours until consciousness returns, is a routine procedure.

Veratrum viride in the form of Veratrone* is used in the following manner according to the authors: "Give 10 minims immediately. Repeat every 10 to 15 minutes until the pulse rate is below 60 or the systolic blood pressure is below 120; thereafter until the patient is conscious, and repeat in 3 to 10 minim doses if pulse rate goes over 80 or the blood pressure 150 systolic; after the patient is conscious and cooperative, give 3 to 10 minim doses if the patient is nauseated, has severe headache, marked visual disturbances, epigastric pain, or convulsions."

The control of convulsions is striking, being effective in 80 per cent of the cases in thirty minutes. When the acute stage is controlled, labor, if not spontaneous, is induced by medical means, or bagging and stripping the membranes. Abdominal delivery was not performed in any case. In our last ten cases with this method no deaths have occurred.

Postpartum hemorrhage is not the serious problem which existed before the advent of safe blood transfusion. One hundred and six private cases were encountered and 54 clinic cases, with no deaths in the former and five in the latter. The use of blood transfusion early and in adequate amounts has prevented many unhappy events. With our recent knowledge of the Rh factor, a serum or warm agglutination test is done in each case requiring whole blood, plasma being used until this information is obtained.

Rupture of the Uterus.—In our recent report of rupture of the uterus in twenty-two cases, 56 per cent occurred in old cesarean scars, 26 per cent followed podalic version, and the remainder resulted from trauma, oxytocic drugs, and one was of unknown origin. Eighteen of these cases were salvaged hysterectomy being the operation of choice in sixteen. Now, it is our practice to have previous sections who have had morbidity, report for section before labor, as we found this was an etiological factor in subsequent ruptures.

Puerperal Sepsis.—A surprisingly low death rate from puerperal sepsis, per se, occurred in our series, only four deaths being encountered. This is probably influenced by restricting our hospital facilities to trained men, with an occasional general practitioner limited to normal deliveries. With the advent of sulfonamides and the recent acquisition of penicillin for civilian use, death from puerperal sepsis should be a rare occurrence.

DR. R. T. LA VAKE, MINNEAPOLIS, MINN.—One of the outstanding lessons to be drawn from these detailed and extensive analyses is the importance of a type of prenatal care that will assure getting abnormal cases to the hospital early, and all cases to the hospital free from infection. Failure in these regards may render futile the best nonoperative or operative treatment.

Women should be convinced that nothing must enter the vagina in the last three months of pregnancy. The importance of this is manifest where one sees infection and no vaginal interference of any kind has been made by the physician. Too many unnecessary vaginal examinations are made by physicians, and too little heed is given to the danger of possible slips in aseptic technique.

For those who handle abnormal cases, this paper is of great importance, because the data, skilfully marshalled, show at a glance the significant frequency with which intervention preceded mortality, and the individual analyses show the dangers inherent in errors of operative choice and technique, and properly emphasize the necessity of preparation for and adequate use of blood replacement; but of even greater importance is the clear and compelling lesson that it holds for all who practice obstetrics, namely, that delayed hospitalization in abnormal cases, and prehospital infection in any case, may render of no avail even the most approved terminal treatment.

*Parke, Davis & Company.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—Dr. Norton deserves a great deal of commendation for this very excellent analysis. It seems to me that one of the important things he has brought out in his paper is this question of preventability. I believe to make that one item of value it should be broken down. When the New York Academy of Medicine brought out their report ten years ago those of us who did the work felt that unless we started with the factor of preventability the report would be of really comparatively little value. It brought about a great many heartaches but still we persisted in our ideas based on three years' analyses, and I believe that such a valuable study on that particular item ironed out more effectively some of the difficulties. The preventability factor should be assessed in accordance with the physician, the hospital, and the patient.

Some of these fatalities are undoubtedly due to the patients themselves because they have not been sufficiently trained to understand their own symptoms or they are too ignorant or too careless. So if you are going to make similar studies of value, you have to break down that preventability factor and state whether the death is due to the doctor, to the hospital, or to the patient. I feel that would greatly increase the value of such extensive and important studies as Dr. Norton has made.

DR. RUDOLPH W. HOLMES, CHARLOTTESVILLE, VA.—It is a significant fact that a staff whose members are imbued with obstetric consciences, and who, with advancing years, have increasing experience and maturing judgment, have lowered maternal mortality enormously. The second basic fact is that maternal mortality is very materially dependent upon the type of service. That obstetric service whose clientele reflects the general characteristics of the community as a whole will naturally have a low mortality rate. In contrast to such are the institutions which receive a disproportionately large number of the lethal complications of obstetrics, and inevitably their mortality rates will be high.

From questionnaires sent to hospitals by the Committee on Child Health and Protection in 1930 it was found that in 489 hospitals with 236,156 births, 1,915 maternal deaths occurred, a rate of 0.819 per cent. Of these, 73 hospitals with 18,088 births had no maternal deaths. One hospital with 97 births lost 7 mothers—7.2 per cent, its excuse being that it had 7 eclamptics, 3 ectopics, and 28 abortions.

The Cook County Hospital of Chicago and the Boston City Hospital are prototypes of certain institutions which are the "dumping grounds" for the neglected, unmanaged, and mismanaged women afflicted with the diverse lethal complications. The inevitable consequence is that the mortality rates are high in comparison with the rates obtaining in hospitals of other types of service; the death rate of 1 to 2 per cent is not excessive when the incidences of pathology are analyzed.

I always have been bitter over the pronouncement that the obstetric services in general hospitals were veritable lazarets and that those in maternity hospitals were sanctuaries. Some years ago (1932) a paper appeared in which this allegation was made, based on the fact that the writers discovered that of 38 "epidemics" of puerperal sepsis, 35 had occurred in general hospitals and only 3 in maternity hospitals. At the time the article was published there were over 4,000 general hospitals which harbored parturients, whereas there were not more than 10, or by a stretch of the imagination 15, veritable maternities.

DR. NORTON (closing).—The possibility that some of these patients came in already infected does not show in the paper because it could not be too definitely established. However, a couple of them admitted that they had cohabited within a few hours of admission to the hospital.

I agree that to break down the statistics properly preventability should be assessed against the private doctor, the hospital, and the patient always.

OBSERVATIONS ON BREECH DELIVERIES IN A GENERAL HOSPITAL*

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THE management of breech presentations, especially in primiparas, has long been a subject of controversy. The advisability of prophylactic external version, the advantages of extraction or spontaneous delivery, are all live debatable subjects. The one uncontroversial, undebatable point is that a breech presentation is a major obstetric complication.

We have analyzed the breech deliveries occurring from Sept. 1, 1930, to March 1, 1944, on the obstetric service of the Millard Fillmore Hospital, a general hospital where an average of 150 operators deliver one or more babies annually. These statistics give a picture which is probably comparable with that of most general hospitals throughout the country where breech cases are not placed under the control of a few selected operators. The fact that we do a greater number of elective internal podalic versions (about 15 per cent) than are done at many institutions has no influence on our results.

We wish to emphasize the fact that the comparison between an elective podalic version and a breech delivery is untenable because in a breech delivery it is impossible to control the arms, the head is always unmolded and is frequently extended. In an elective internal podalic version these three uncontrollable complications can be avoided.

During the period mentioned, there were 23,916 patients delivered at the Millard Fillmore Hospital with 786, or 3.2 per cent, having babies presenting by the breech, of which 455 were primiparas and 331 multiparas. Forty-eight of the infants were one of twins or triplets, while eleven mothers had two babies presenting by the breech, making a total of 797 infants. These latter will be considered as single breech deliveries in order to equalize the number of babies and mothers.

There were 121 (15.3 per cent) weighing less than 5 pounds. This is two to three times greater than the incidence of premature infants in total births as cited by Greer and Lussky,¹ Holtz,² Stone,³ or Mauzey.⁴ Holtz² states, however, that "abnormal presentation, such as breech occurs much more frequently among premature babies than among those at full term." Mauzey⁴ cites a breech incidence of 11.2 per cent for premature babies and stresses that "the danger of breech delivery

*Read at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1944.

in the premature infant is not generally appreciated." He reports a fetal mortality in such cases of 43.4 per cent.

There were fourteen instances (1.6 per cent) of prolapsed cord. This is almost four times the average incidence of 0.44 per cent for reports made in 1940, and considerably above that of 0.92 per cent for reports between 1907 and 1922, as quoted by Bourgeois.⁵

The following methods of delivery were employed and the corresponding gross fetal mortality is shown in Table I.

TABLE I

	BREECH EXTRACTION NO. PER CENT	SPONTANEOUS EXTRACTION NO. PER CENT	SECTION NO. PER CENT
All cases	677 (86.15)	24 (3.05)	85 (10.80)
Fetal mortality	142 (20.90)	6 (25.90)	0
Primiparas	374 (82.20)	13 (2.85)	68 (14.95)
Fetal mortality	80 (21.40)	4 (36.30)	0
Multiparas	303 (91.50)	11 (3.32)	17 (5.12)
Fetal mortality	67 (21.10)	2 (18.10)	0

A total of 150 infants were either stillborn (96) or died in the neonatal period (54), a gross fetal mortality of 19.2 per cent. Excluding 74 "nonviable" infants (i.e., infants weighing less than 3 pounds, macerated infants, or monstrosities), there are left 76 fetal deaths for a corrected fetal mortality rate of 9.6 per cent.

For the 455 primiparas this is a corrected rate of 9.6 per cent (49 infants) and for the 331 multiparas 8.1 per cent (27 infants). The causes of these 76 fetal deaths are shown in Table II, autopsy being performed on 54 infants.

TABLE II. CAUSES OF FETAL DEATH

	PRIMIPARAS	MULTIPARAS
Proved cerebral damage	21	8
Clinical cerebral damage	15	2
Prematurity (autopsy)	5	6
Prematurity (all under 4½ pounds, no autopsy)	2	4
Asphyxia (prolapsed cord)	2	4
Bronchopneumonia	1	2
Erythroblastosis	0	1
No cause found at autopsy	3	0

This shows that 36, or 75 per cent, of 48 fetal deaths in the group of infants of primiparas having breech presentations, and 10, or 34.4 per cent, of 27 fetal deaths in the group of infants of multiparas having breech presentations were due to cerebral damage sustained during delivery. Also, since premature delivery and prolapsed cord are such common complications of breech presentations, we feel that all but 9 of the 75 fetal deaths can be justly attributed to the breech presentation or delivery.

There were seven maternal deaths among the 786 patients of this series. Five were primiparas, two were multiparas. This is a rate of 0.89 per cent, considerably above our average maternal mortality rate. A brief summary of these deaths follows:

CASE 1.—M. J., 31 years old, primipara, "contracted pelvis." Membranes ruptured spontaneously on admission. Four-hour test of labor. High classical section. Living female infant 7 pounds, 12 ounces. First two days post partum uneventful. Third day increased pulse, elevated temperature, distention. Progressive course to exitus on sixth day. Autopsy: Acute suppurative endometritis, generalized acute peritonitis.

CASE 2.—B. G., 20 years of age, primipara. Only pelvic measurements recorded 23-28-33-20. Membranes intact. Duration of labor not stated. Breech extraction. Living female infant, 8 pounds, 10 ounces. Cyclopropane anesthesia. Vomited twice during delivery. Fundus firm at umbilicus following delivery. Pulse imperceptible on return to room. Expired thirty minutes after delivery without recovery consciousness. No autopsy.

CASE 3.—I. H., 23 years old, primipara. Only pelvic measurements recorded 23-28-33-19. Membranes ruptured forty-eight hours and labor for seventy-two hours. Attempted delivery in home. Brought to hospital and extraperitoneal section performed. Living male infant, 9 pounds, 12 ounces. Distention, elevated pulse, septic temperature post partum. Exitus fifth day. No autopsy.

CASE 4.—L. L., 38 years old, para ii, "contracted pelvis." Difficult breech delivery five years ago resulting in death of baby. Membranes intact. Elective low cesarean section. Living female child, 7 pounds, 4 ounces. Postpartum course uneventful until twelfth day when patient complained of severe pain in chest. Expired suddenly. No autopsy. Diagnosis: Embolism.

CASE 5.—L. F., 39 years old, para iii. Membranes ruptured spontaneously. Duration of labor four hours. Breech extraction. Stillborn female weighing 4 pounds, 11 ounces. Patient had been treated for cold prior to admission. Temperature 99° F.; pulse 90; respirations 28. First postpartum day, temperature 100° F., pulse 120, respirations 30. Examination of chest—dullness in left axillary and posterior lung field. Sulfathiazole, 1 Gm. every two hours. Forced fluids. Second day, temperature 103° F. Progressive course to exit on second day. No autopsy.

CASE 6.—H. E., 27 years old, primipara. X-ray films showed frank breech presentation. Large fetus in right sacrum posterior position (pelvis adequate?). Membranes intact. Eighteen-hour labor. Breech extraction. Living male infant weighing 9 pounds, 3 ounces. Condition of mother and baby satisfactory. Patient sent to room. One hour later patient was flowing moderately. Uterus soft and boggy. Returned to delivery room, given intravenous fluids, blood, and ergotrate. Uterus and vagina packed. Bleeding continued. Patient expired two hours later. Diagnosis: Postpartum hemorrhage.

CASE 7.—M. H., 45 years old, primipara. Membranes intact. Duration of labor eighteen hours. One hour prior to delivery patient was given subcutaneous pituitrin 2 minims at fifteen-minute intervals for

three doses. Contractions became very forceful. Breech extraction. Living female infant weighing 7 pounds, 8 ounces. Condition fair. Patient returned to room. Flow moderate. Uterus soft, boggy. Given intravenous plasma, blood, ergotrate. Returned to delivery room. Cervix repaired. Uterus packed. Bleeding continued. Expired three hours after delivery.

Besides fetal and maternal deaths, the following maternal injuries were sustained: 13 third-degree lacerations of the perineum, 123 second-degree tears, 130 first-degree lacerations; 60 episiotomies were made.

The maternal morbidity rate (temperature of 100.4° F. or over, in any two consecutive twenty-four-hour periods, excluding the first twenty-four hours following delivery) was 11.5 per cent. This is almost three times the morbidity rate reported recently by one of the authors⁶ in a series of 1,000 consecutive deliveries at the same institution.

Discussion

With such a picture the importance of improving the chances for a successful termination in breech presentation is obvious. Prophylactic external version during the latter months of pregnancy is only successful in certain cases, and thus can be no more than a partial solution. We have had no experience with it personally. As between the conservative and activist methods of treatment of breech presentations, we definitely adhere to the latter. It is our practice to frequently elect cesarean section in breech cases, particularly in primiparas. We also cesareanize those breech cases whose previous deliveries were fatal to the babies. This may appear radical to some of the profession, but we feel that a breech presentation presents, particularly in the cases with a borderline pelvis, one of the gravest problems in obstetrics, and that the obstetrician, in these borderline cases, is not justified in subjecting a baby to possible birth injuries and the mother to the possible loss of her baby. In this series, eighty-five sections were done with no fetal mortality.

If we do decide upon a pelvic breech delivery, after careful consideration of the risks involved, we convert the breech, under deep anesthesia, into a double footling and extract slowly, after making sure that the lower uterine segment is effaced and the external os completely dilated. The following is our technique:

After careful ironing out of the vagina, the operator's hand with the palm up is introduced into the relaxed uterus and the buttocks are pushed up out of the inlet, both feet are grasped and brought down until the knees are exposed. The buttocks are delivered through the hollow of the sacrum by lifting both feet up toward the ceiling. The direction in which the buttocks will rotate depends upon the original position. Traction upon both feet will complete the rotation so that the back of the baby is straight across under the pubic arch. It is

most important that the operator does not rush the delivery. The setting of a time limit and the custom of having a nurse count off the minutes from the time the umbilicus appears at the perineum is pernicious and definitely outdated.

Both shoulders are delivered as anterior shoulders and, if the arms are not extended, a finger is placed in the bend of the elbow to deliver them. Whether or not the arm or arms are extended is a matter of luck and lack of haste in the extraction. This is unlike a podalic version and extraction where in every case it is possible and necessary to fold the arms before the version is attempted, and thereby completely avoid the serious complication of extended arm or arms.

Realizing that in the majority of cases extension of the head to some degree is always present, an attempt is made to flex the head by external pressure above the symphysis. It is then rotated to a transverse position, pushed through the inlet as such, and later rotated back to an anterior-posterior position for extraction. Piper forceps applied to the sides of the baby's head with the handles depressed (lowered) before the forceps are locked, many times aid in increasing the flexion of the head, and in the extraction.

In recent years, we not only have stressed the inherent dangers of breech presentation and encouraged a more active treatment of those with borderline fetopelvic disproportion, but we have also emphasized making the head and arms the x-ray target while x-raying the pelvis.

The period of 1939 to 1940 is typical. In this time there have been 67 patients with infants presenting by the breech, consisting of 36 primiparas and 31 multiparas. There were no maternal deaths, but seven fetal deaths, a gross mortality rate of 10.4 per cent. Five of these can be classified as "nonviable," as described above. This gives a corrected fetal mortality rate of 2 per cent, which is about the hospital average. The two infants that died showed evidence only of prematurity, one weighing 31.2 ounces and the other 3 pounds, 15 ounces, at birth. Mothers of both were multiparas and both infants were delivered by breech extraction.

Table III shows the methods of delivery used in breech cases and the corresponding gross fetal mortality for the year, Sept. 1, 1939, to Sept. 1, 1940.

TABLE III

	BREECH EXTRACTION		SPONTANEOUS BREECH		SECTIONS	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
All cases	57	(85.0)	3	(4.5)	7	(10.5)
Fetal mortality	7	(12.3)	0		0	
Primiparas	27	(75.0)	2	(5.6)	7	(19.4)
Fetal mortality	1	(3.7)	0		0	
Multiparas	30	(96.8)	1	(3.2)	0	
Fetal mortality	6	(20.0)	0		0	

There were no third-degree lacerations of the perineum, thirteen second-degree lacerations, sixteen first-degree lacerations, and two episiotomies. The maternal morbidity was 10.4 per cent (seven cases) and seven days was the maximum duration of morbidity in any case.

The fact that we delivered almost one primipara out of five by cesarean section may seem very radical. All these were elective sections, however, done under the most ideal conditions, and the average weight of the seven babies was 8 pounds, 14 ounces.

Summary

1. Of 23,916 patients delivered during 13.5 years on the obstetric service of a general hospital, 3.2 per cent had babies presenting by the breech.

2. Thirteen and six-tenths per cent of the infants weighed less than 5 pounds, and prolapsed cord occurred in 1.6 per cent of the cases.

3. There was a gross fetal mortality of 17.4 per cent, with a corrected fetal mortality of 9.6 per cent. For primiparas this corrected fetal mortality was 9.6 per cent and for multiparas 8.1 per cent.

4. We feel that 79 of the fetal deaths, including 46 due to cerebral damage, can be justly attributed to the breech presentation or delivery.

5. There were 7 maternal deaths.

6. There were 13 third-degree, 123 second-degree, and 130 first-degree lacerations, and 60 episiotomies.

7. The maternal morbidity was 11.5 per cent.

Conclusion

1. Breech presentation is a major obstetric complication with a high fetal and maternal mortality and a high maternal morbidity.

2. In breech presentation prematurity occurs about two to three times more often and prolapsed cord about four times more often than in pregnancies in general.

3. Breech extraction demands recognition of complete effacement of the lower uterine segment and proper dilation of the external os.

4. Remembering that the head is not molded, is usually extended, and that the arms cannot be controlled, is of fundamental importance.

5. Haste is unnecessary and often fatal to the baby.

6. Making the head and arms of the fetus the x-ray target is an important adjunct in determining type of procedure to be followed.

7. The more common use of elective cesarean section as a method of delivery in breech presentations, especially in primiparas with borderline fetopelvic disproportion, is advocated.

References

1. Greer, R. M., and Lussky, H. O.: AM. J. OBST. & GYNEC. 30: 669, 1940.
2. Holtz, S.: Ibid. (Abst.) 38: 178, 1939.
3. Stone, E. L.: The New-Born Infant, Philadelphia, 1938, Lea & Febiger, p. 270.
4. Mauzey, A. J.: AM. J. OBST. & GYNEC. 30: 295, 1940.
5. Bourgeois, G. A.: Ibid. 41: 837, 1941.
6. Erving, H. W., and Meister, E. F.: Ibid. 42: 326, 1941.

Discussion

DR. JAMES L. REYCRAFT, CLEVELAND, OHIO.—Dr. Potter has not emphasized the elderly primipara as much as we do. We believe that an elderly primipara with a breech presentation offers real trouble. The result is that we are more inclined to section those patients than the young primipara with adequate measurements. In a young primipara with adequate measurements we have in the past delivered them as such without much thought, but it has often brought a lot of problems.

Very little has been said about x-ray pelvimetry but I think it has a place in this study. It is a well-known fact that you cannot compare the head with the pelvis when the head is not in or near the pelvis, but you can get a fair idea of pelvic size and shape.

I believe that a suitable episiotomy is important. It is known that Dr. Potter does not favor that, but the type of episiotomy that is best done by the operator should be utilized, and a very adequate one will aid in the delivery of the aftercoming head.

The contractions of the bony outlet give us more trouble sometimes than the soft parts, and there pelvimetry is valuable. So that, given a breech, whether a footling or a full breech, in a pelvis of certain proportions, it is up to the individual operator to decide whether or not that patient should be delivered by the usual methods.

DR. WILLIAM T. McCONNELL, LOUISVILLE, KY.—There are two things that I wish to emphasize in handling breech deliveries. One is a technique that is adequate and safe for the patient. We use Dr. Potter's technique in our clinic and in our private practice and find it very satisfactory. In fact, there is nothing in the textbooks that I have ever found that compares with it so far as safety in breech presentation is concerned.

The next important thing is estimation of disproportion. It is extremely difficult to get adequate x-ray information as to the proportion of that given child and the given pelvis, because of magnification. I will show you how we get around that. We have used it as our guidepost and the results have been excellent. We stand the patient up before an x-ray machine and take two views, one straight through the abdomen and the other through the back. We measure the head and the transverse diameter of the pelvis. From the anteroposterior view it would look as if the head had plenty of room; but from the anterior-posterior it looks like a hydrocephalic. We add the two diameters of the head, divide by two, add the two diameters of the pelvis and divide by two. If the average diameter of the head is greater than the average diameter of the transverse of the pelvic inlet, we conclude there is definite disproportion. This is so simple that it sounds silly but it works on the law of averages and I submit it for what it is worth.

In the case of elderly primiparas or the borderline pelvis, which we check by this x-ray method, we do not hesitate at all to do cesarean section. We believe that it is not only advisable but the best method of procedure in a questionable breech delivery because of the incidence of birth injuries to the child and also of fetal mortality.

DR. JAMES K. QUIGLEY, ROCHESTER, N. Y.—Dr. Potter has done well to emphasize the effacement of the lower uterine segment and to condemn speedy delivery. He is reporting cases done at a hospital with a large courtesy attending staff which brings out the importance of consultation in all abnormal cases. In the hospitals in Rochester, consultation is considered necessary in cases of breech delivery. I should like to make a plea for conservative treatment in the delivery of frank breech rather than routinely decomposing or bringing the feet down when such management results

in a mortality of 5.7 per cent in 140 cases. I believe that vis a tergo is better than a pull from below.

DR. WILLIAM R. BARNEY, CLEVELAND, OHIO.—I would like to ask why they did not do more episiotomies? We make it a rule that episiotomy is obligatory in all breech presentations. I think it is a mistake not to do it.

DR. ARTHUR H. BILL, CLEVELAND, OHIO.—So far as the cephalopelvic disproportion is concerned I agree with Dr. Potter. If there is reasonable doubt that the head will go through, a cesarean should be done.

I would like to stress again the need of making the way clear for the passage of the baby all the way from the lower uterine segment down through the vaginal outlet. We cannot take for granted that there is complete dilatation of the cervix just because the breech has passed through the os. Even if it is protruding through the vulva that does not mean that there is full dilatation. If one proceeds with the delivery without taking into consideration the condition of the cervix, he may get into trouble. I always like to stress the fact that nothing should be taken for granted, but that one should always feel the cervix and make sure that it is wide open. I believe the greatest single cause of casualties in breech extractions is due more to resistant soft parts and the lower uterine segments than to the bony pelvis because we usually decide in advance about the bony pelvis.

I agree with what Dr. Barney says, that the episiotomy is a great child saver, but above all make sure that the cervix is dilated.

Very little is said about the anesthetic. I think that plays a great part in breech extractions. There should be as deep anesthesia for breech extraction as for podalic version.

I do not quite agree with Dr. Potter that whether the arms go up or not is a matter of luck. My opinion is that the reason they go up in breech extraction is that the lower segment of the uterus is tight and the arms are forced up. Therefore we should make sure that the os is fully open, and I feel that complete anesthesia is most important for the breech extraction.

DR. L. A. CALKINS, KANSAS CITY, KAN.—For a number of years I have taught my students that the presence of a skilled assistant in breech delivery is more important than the presence of such at a cesarean section. This guidance of the head from above, both to improve the flexion as Dr. Potter has pointed out, and to offer some additional force of a modified kind as referred to by Dr. Quigley, is much less conducive to injury to that head than too much traction from below. In fact, it is not possible to pull from below, if I understand the anatomy, in the direct axis of the pelvis. I would like to hear Dr. Potter comment upon this point further. Whenever I do not have skilled assistants available, I use whatever assistance I have for the delivery from below and myself do the guidance from above and feel that I am rendering my patient better service thereby.

DR. WARD F. SEELEY, DETROIT, MICH.—I have been very much interested in Dr. Potter's paper inasmuch as I have had occasion to review our breech cases from a standpoint of the fetal risk not long ago. We find that the fetal risk in breech deliveries is higher than one would expect.

A high percentage of breech positions will deliver spontaneously if allowed to proceed in labor. It is my practice to allow labor to proceed in these cases until there is an actual indication for interference. In other words, I do not believe it is necessary or advisable to do routine breech extraction. The fetal risk in breech is sufficient, I think, to warrant a thorough trial of external version in the last months of pregnancy. This should be done without anesthesia. In elderly primiparas with large babies, cesarean section should be considered in the interest of a particularly desirable child.

DR. J. P. GREENHILL, CHICAGO, ILL.—Dr. Potter spoke of a “test of labor” in the first fatal case he reported. We should use the term “test of labor” only in head presentations and no other.

I fully agree that in every case of breech presentation in a primipara, or a multipara, a general practitioner should have consultation with a specialist. This consultation should consist not only of advice but also of the actual delivery of the baby by the specialist.

I agree, also, that more cesarean sections should be done in elderly primiparas with breech presentation. It was unfortunate that in the last fatal case recorded by Dr. Potter, a cesarean section was not done. The patient was 45 years old. In view of the history of severe bleeding, the necessity for repairing the cervix, and the fatal outcome, the patient most likely had a rupture of the uterus. It is too bad that there was only one autopsy among the seven maternal deaths.

DR. POTTER (closing).—I would like to emphasize the fact—and I am sorry I do not agree with Dr. Barney and Dr. Bill—that the position of the arms is very important. From a practical standpoint, when you have your pelvic x-ray taken, pay a little attention to the position of the arms, and if the arms are behind the head or alongside the body, and if you have a markedly extended head, regardless of whether your measurements of the head and pelvis are normal, it would behoove you to think of a cesarean section in that case. We have had considerable experience, I think, with extraction of arms and aftercoming heads, and I am frank to admit that a breech delivery is one of the most serious things that we come in contact with.

I agree with Dr. Quigley about the importance of consultation. It seems that in all hospitals, particularly in general hospitals, the rule of consultation is there, but the following of the rule is not carried out and many of the poor results are due to the fact that the obstetricians themselves, not daring to hurt the feelings of the man handling the case, get careless in their advice.

Certainly in any case where there is a reasonable doubt, regardless of whether the patient is young or old, she deserves a section. We too believe that the secret of success is getting rid of the resistance of the soft parts, meaning the lower uterine segment and the cervix, and if the patient is allowed to go into labor, those soft parts will give you much difficulty in the extraction, particularly of the arms.

We also believe, as Dr. Calkins does, that the presence of an assistant is very helpful and always necessary. We insist on having the resident scrub up with us and consider his assistance very important.

The term “test of labor” was not my term. It was a term taken from the chart of that particular case.

I am of the opinion that no patient with breech presentation, after complete dilatation of the external os, should be allowed to progress into the second stage of labor.

A CRITICAL ANALYSIS OF TWENTY-TWO YEARS' EXPERIENCE WITH CESAREAN SECTION*

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WILLIAMS,¹ in 1921, presented the Jerome Cochran Lecture before the Alabama State Medical Association. This lecture made an early impression and was a critical analysis of 183 cesarean sections in a series of approximately 20,000 deliveries at The Johns Hopkins Hospital. The conclusions drawn from this epoch-making study rank with the work of Sanger² as a distinct advancement in the care of the obstetric patient.

From March 1, 1922, to June 1, 1944, inclusive, I performed 362 cesarean sections in a series of 5,975 term or near-term deliveries. This study consists of private cases only and for all practical purposes, the operations were performed by one individual. Except for one case, all the patients were white. From such a limited experience no hope is entertained that anything new will be added to the cesarean section problem. However, it should be of interest to review the work of one individual, especially since most of our knowledge about cesarean sections has been based on mass statistics from the work of groups of obstetricians in large clinics.

When it is considered that 362 cesarean sections in 5,975 deliveries gives an incidence of 6 per cent, or 1 in 16.5 cases, one is alarmed by the high percentage of major operative deliveries. However, it is reasonable to assume that any physician limiting his work to obstetrics would attract a larger number of complicated cases and that an accumulation of such cases over a period of two decades would increase the incidence of cesarean sections by the number of *repeated* cesarean sections alone. In the early twenties most of the obstetrics in practically all communities in Texas was done by general practitioners and the surgeon was called when a cesarean section was *considered* necessary. This was particularly true in Houston.

Davis,³ in April, 1929, reported that: "In the city of Houston from 1923 to 1926 there were 107 cesarean sections done at two hospitals. The patients came from the private practices of general practitioners, general surgeons, and obstetricians of the city. The maternal mortality following these operations was 14.4 per cent. Fifty-one of the 107 patients were operated upon by a group of recognized surgeons and by physicians in general practice with a maternal mortality of 33 per cent. The other 56 patients were delivered by a small group of

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physicians specializing in obstetrics and by surgeons closely associated with them, with a maternal mortality of only 1.8 per cent."

In an address before the Sloane Hospital Alumni in 1928, Williams⁴ pointed out that "a considerable fraction of the excessive risk in child-birth is due to unnecessary resort to cesarean section by those who do not realize its dangers and limitations." He also cited the high mortality in Houston to show that judgment as to the time when to and when not to do a cesarean section is far more important than the surgical skill in performing the operation, concluding that a number of women had been sacrificed to ignorance. In 1930 Smith and I⁵ reported two series of cesarean section cases in Houston, Texas, showing definite improvement in maternal mortality in one three-year period over a previous three-year period. It was concluded that "while the indications for cesarean section are well known, the profession at times tends to ignore them, with a resulting increase in morbidity and mortality" and also that "the ultimate well-being of the patient depends less on the surgical skill of the operator than on the obstetric judgment he displayed before picking up his scalpel." Reference is made to all these facts in order to indicate the status of cesarean section in this specific community. These facts also explain why there was a definite trend to have the obstetrician perform the cesarean section rather than the general surgeon.

TABLE I. TYPES OF CESAREAN SECTION PERFORMED

TYPE OF OPERATION	NUMBER OF CASES
Laparotrachelotomy	247
Classical	106
Laparotomy with repair of ruptured uterine scar	2
Cesarean section with hysterectomy	7
Total	362

The type of operation employed depended largely on the individual case. Laparotrachelotomy was most frequently chosen and the convalescence following it has been found to be exceptionally free from any discomforts. Moreover, abdominal distention has been negligible, and with repeat cesarean sections practically no adhesions have been encountered. These results have not been generally observed in the cases where the classical type of operation has been carried out.

The classical type of operation adapts itself very favorably to local anesthesia and to those cases in which speed is paramount. The convalescence has been noticeably uneventful in the few patients in whom hysterectomy followed cesarean section, and no difficulties were experienced in carrying out this procedure. It has been our practice to refrain from delivering the uterus through the abdominal incision and from using abdominal packing. Contraction of the organ has been obtained in practically every case by the use of pituitary extracts and ergot derivatives as soon as the uterus has been emptied. Attention should be called to the fact that no extraperitoneal cesarean sections are included. No doubt there have been some indications for such a type of operation, but only during the past year has the technical difficulty of the operation been surmounted.

Formerly it was the rule not to give any preliminary medication except atropine. It is still a question whether such a strict policy is necessary. Our impression during the past few years has been that by using small doses of sedatives, induction of anesthesia has been made easier, and no interference has resulted with the initiation of the child's respiration, provided the anesthetist was experienced in giving obstetric anesthetics and the infant was mature. Blossom⁶ believes that the contractions of labor "condition" the baby's respiratory center and those babies born *per vaginam* or by cesarean section after some labor are less likely to need resuscitation than those where cesarean section is performed prior to the onset of labor. The degree of anesthesia, particularly when morphine is used for premedication, determines above all other factors the need for resuscitation of the infant after cesarean section. While a combination of nitrous oxide and ether has been the anesthetic agent most frequently employed in this series, it has also been associated with the greatest number of maternal deaths. In the two cases of death from shock or circulatory collapse, it is difficult to say that the anesthetic was the fatal factor; however, hemorrhage was not the cause of death, as shown by the clinical history of slight loss of blood and at autopsy where well-contracted uteri were found in both instances. The importance of shock and hemorrhage as a cause of maternal deaths in connection with cesarean section has been emphasized by Eastman and associates.⁷ It can be definitely stated that in the other two cases the nitrous oxide-ether anesthetic played no part in the causation of death. While cyclopropane was employed in only twenty-three patients, yet one death may be attributed to its use. In another instance, difficulty in the form of temporary cessation of respirations and marked cyanosis was experienced during its administration. I adhere to the view expressed by Beecher,⁸ namely, that cyclopropane is a "... potent anesthetic. Low concen-

TABLE II. TYPE OF ANESTHETIC EMPLOYED

ANESTHETIC AGENT	NUMBER OF CASES	MATERNAL MORTALITY		
		NUMBER	UNCORRECTED PERCENTAGE	CORRECTED PERCENTAGE
Nitrous oxide-ether	244	4*	1.64	0.82
Ethylene	18	0	0.00	0.00
Cyclopropane	23	1†	4.35	4.35
Spinal procaine	23	2‡	8.70	0.00
Local infiltration	51	1§	1.96	0.00
Chloroform	3	0	0.00	0.00
Total	362	8	2.21	0.83

*1, Elderly primipara with death due to shock; 2, repeat cesarean section, twins, death due to shock; 3, melano sarcoma with generalized metastases; death thirty-three days later; 4, known sensitivity to a sulfonamide; convulsion followed by hyperpyrexia and anuria after sulfathiazole intravenously on the fourth postoperative day.

†1, Asthmatic elderly primipara; died of pneumonia on third day.

‡1, Class IV heart disease, seen late in pregnancy; lived twenty-four days after operation; 2, multipara with advanced chronic nephritis; hospitalized for seventeen days to obtain a viable fetus; died twenty-seven days after operation, cerebral hemorrhage.

§1, Moribund primipara with cavernous sinus thrombosis; delivered to salvage fetus.

tration in the central nervous system does not provide a degree of muscular relaxation comparable to that produced by ether at a safe level of anesthesia." These untoward effects occurring with cyclopropane anesthesia in the current series call to mind the incompatibility of pituitrin and cyclopropane reported by Belinkoff.⁹

While there have occurred no difficulties with the use of spinal anesthesia in twenty-three patients, it is believed that spinal is not absolutely free from danger. The risks can be reduced to a minimum by careful selection of patients and by using as small an amount of the drug as possible (100 to 150 mg. procaine). The two deaths occurring after the use of spinal anesthesia were in no way associated with this type of anesthetic. The excellent results reported by Cosgrove and Norton¹⁰ speak most favorably for the use of spinal anesthesia for cesarean section.

Local infiltration is considered the anesthetic par excellence and should be employed more frequently. The time required to perfect the technique of local anesthesia would more than recompense one in the good results obtained. This is borne out by the low maternal and fetal mortality rates reported by Schumann¹¹ and others.

With a greater demand for trained anesthetists in obstetrics, and with the rapid development of anesthesia as a specialty, no doubt one will find that a competent, well-trained anesthetist is as important as the type of anesthetic agent used.

In determining the indication for a cesarean section, one should consider the patient "as a whole"; namely, her age, history of previous labor, condition of cervix, and position of fetus, as well as future chance of childbearing, in addition to the true obstetric indication. In private practice this complete knowledge of the patient often tends to place too high a value on the child, while in the clinic case the tendency may be in the opposite direction and labor may be considered

TABLE III. INDICATIONS FOR CESAREAN SECTION

INDICATION FOR CESAREAN SECTION	NUMBER OF CASES	MORTALITY	
		MATERNAL	FETAL
Dystocia	247	4 (1.62%)	5 (2.02%)
Cephalopelvic disproportion	160		
Diabetes and fetus of excessive size	2		
With previous cesarean section	66		
Extensive birth canal repair	19		
Hemorrhage	23	0	4 (17.4%)
Ablatio placentae	6		
Heart disease	11	1 (9.09%)	0
Previous cesarean section with suspected weak uterine scar	15	0	0
Ruptured uterine scar	2	0	2 (100%)
Interest of baby	8	2 (25%)	0
Sterilization (active tuberculosis)	1	0	0
Toxemia of pregnancy	55	1 (1.82%)	5 (9.09%)
With convulsions	13		
Without convulsions	42		
Total	362	8 (2.21%)	16 (4.42%)

as a purely mechanical problem, thereby often minimizing the risk to the infant. At any rate, each case should be judged on its own and complete individual merits and the obstetrician, cognizant of the two schools of action, can only hope to develop an "obstetric conscience," which is the ultimate objective to be desired. Every patient in this series has had the benefit of one or more consultations. It has been rather striking that in a relatively large number of our patients, as Falls¹² pointed out in his series, there has been a multiplicity of factors which has helped in making the decision to perform the cesarean section in addition to the single indication to which the operation has been ascribed.

The definite cephalopelvic dystocia cases require very little consideration and the patient should be operated at an appointed time. In spite of the danger of infection associated with labor and premature rupture of the membranes, a trial labor of from six to ten hours has frequently been allowed in the questionable or borderline cases, with apparent satisfactory results. In the light of the work of Stander and Douglas¹³ on intrapartum infection, this policy might be considered unwarranted; however, there has occurred no death from septicemia or peritonitis in this series. No doubt, in clinics where the technique of x-ray pelvimetry has been highly developed, as Kellogg¹⁴ points out, the incidence of cesarean section for cephalopelvic disproportion has been decreased; however, it has been generally felt that the aid given by the average roentgenologist to the obstetrician in such cases has often been misleading. There were five fetal deaths from cephalopelvic disproportion in this group, giving a fetal mortality of 2 per cent. In three instances, however, congenital anomalies were present which were incompatible with life of the infant, thus giving a corrected mortality of 0.81 per cent.

In the seventeen cases of placenta previa, multiparity was only slightly predominant (10 to 7). There were no maternal deaths in this group while the one fetal death was due to a congenital anomaly. In one case of placenta previa centralis, the infant was a Mongolian idiot. The value of x-ray in these bleeding cases to rule out congenital bony deformities of the fetus, as pointed out by Greenhill,¹⁵ and the necessity to have available blood to combat shock from hemorrhage need no comment. It should be further emphasized that the clinical history of vaginal bleeding alone is not sufficient evidence from which to make the diagnosis of placenta previa. Every patient with vaginal bleeding should have the benefit of soft tissue localization of the placenta and careful sterile vaginal examination in an appropriate setting in order to make a definite diagnosis.

Although the six patients with ablatio placentae survived, the outcome to the infants was discouraging. Two infants, weighing over 4 pounds, died shortly after delivery, while an error in auscultation of the fetal heart tones in another patient led to the abdominal delivery

of a macerated infant. Of the remaining three liveborn babies, one sustained a cerebral hemorrhage in utero from anoxia, resulting in spastic paraplegia. In only two of the six patients with ablatio placentae were healthy children delivered by cesarean section. After obtaining such poor results for the child, one naturally would agree with Irving,¹⁶ that delivery *per vaginam* would be the usual proper treatment in these cases.

Cosgrove and Conway have pointed out, however, that the management as between vaginal and abdominal delivery in these cases should be predicated on maternal rather than fetal results.

In forty-six primiparous cases, in addition to other indications, the patient was over 35 years of age. While being an elderly primipara is never per se an indication for cesarean section, it may play an important secondary role in influencing one to perform a cesarean section.

In eleven cases in which the patients had severe cardiac disease there were no fetal deaths, but one mother died twenty-four days post partum from a decompensated heart. This patient, having been seen only two weeks previously, was delivered under local anesthesia at the thirty-sixth week of gestation. Autopsy findings showed that the operation played no part in the causation of death, that is, death was due to myocarditis.

There were eighty-three cases of repeat cesarean section, yet in only fifteen of these patients was the operation performed solely because of a suspected weak uterine scar. There were no fetal nor maternal deaths in these fifteen cases; however, in one instance a partial rupture of the uterine scar was found. In the other two patients with frank uterine rupture, a classical cesarean section had been performed previously and the puerperia had been febrile. These two patients with ruptured uterine scar had their original cesarean sections in 1923 and 1926, during which time it was the practice for the obstetrician to make the incisions and remove the infant while the closure of the uterine and the abdominal incisions were taken over by the general surgeon. Moreover, in the first twenty-seven patients of this series, that policy was in vogue, but since then I have performed the entire operative procedure. These three cases, then, give an incidence of less than 1 per cent of rupture of a previous cesarean scar, but it is believed that this low incidence might have been even lower if more care had been taken in approximating the cut surfaces of the uterine wall. It may be of interest to note that of the total number of patients delivered by me, twenty-three women who had previously been delivered by cesarean section were later delivered through the natural passages.

In eight of the 362 cases, the cesarean section was performed primarily for the safety of the child. Prolapse of the cord through a partially dilated cervix in four patients resulted in four live babies from cesarean section. Two mothers who were near term and doomed to die were delivered of live children by operative procedure. Likewise, two mothers with tragic obstetric histories whose bloods were Rh negative and who had Rh-positive husbands were delivered of live babies at the thirty-sixth week of gestation. Both babies had severe anemia and were of the icterus gravis type at birth but survived after several transfusions.

Under local anesthesia, a primipara with advanced tuberculosis was delivered by cesarean section in order to accomplish sterilization. In addition, there were 33 other instances of sterilization incidental to the

procedure and so far no pregnancies have been known to have occurred in these patients.

It is generally considered radical obstetrics to treat toxemias of pregnancy by major operative procedures, especially if convulsive seizures are present, yet in fifty-five patients with toxemia cesarean section was performed with gratifying results. In thirteen patients with convulsions, in whom the condition was becoming worse in spite of the usually accepted medical treatment, cesarean section was performed under either local or spinal anesthesia with no maternal deaths and only one child, who weighed just 3 pounds, failed to survive. In forty-two patients with severe pre-eclampsia alone or superimposed upon nephritis, the condition of the patient was rapidly becoming worse, so cesarean section was decided upon. The one maternal death occurring twenty-seven days post partum was shown by autopsy to have been in no way attributable to the operation. The study of the weight of the infants gives some very interesting findings.

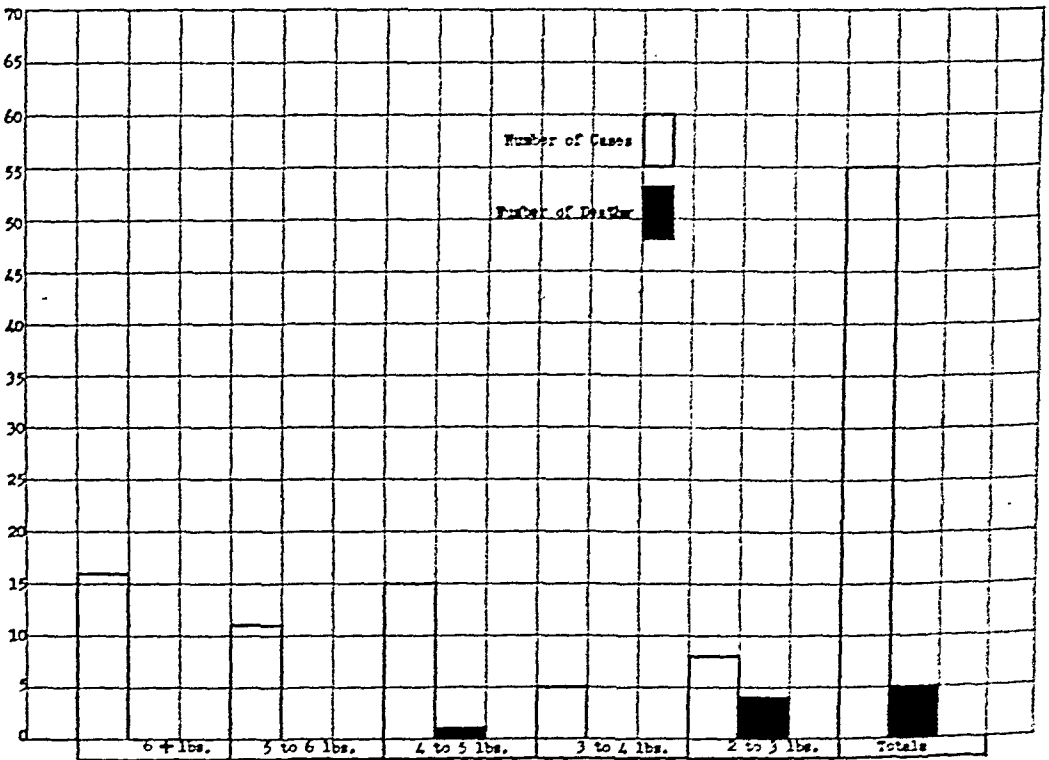


Fig. 1.—Outcome to babies from mothers with toxemia.

Even though the number of toxemia cases is limited, it is interesting to note that only one baby which weighed more than 3 pounds succumbed. Since only one-half of the babies that weighed between 2 and 3 pounds were salvaged, justification for cesarean section in this early period of gestation naturally arises.

There occurred sixteen fetal deaths in 362 deliveries which netted 364 children, that is, a gross fetal mortality of 4.4 per cent. This clearly demonstrates that cesarean section does not always insure a live, healthy baby. However, if we may be allowed to subtract the unavoidable deaths, namely, four infants with congenital deformities

(not bony) which were incompatible with life, two fetuses that died as a result of intrauterine asphyxia from ruptured uteri, four infants in the toxemia group who were quite premature (3 pounds or less), and one macerated infant delivered due to an error in auscultation, there remain only five infants who might have survived, or a corrected fetal mortality of 1.4 per cent.

TABLE IV. CAUSES OF FETAL DEATHS CLASSIFIED ACCORDING TO
MATERNAL COMPLICATIONS

INDICATION FOR CESAREAN SECTION	NUMBER OF CASES	FETAL MORTALITY	
		UNCORRECTED	CORRECTED
Toxemia	55	5* (9.1%)	1 (1.8%)
Hemorrhage	23	4† (17.4%)	2 (8.7%)
Dystocia	247	5‡ (2.0%)	2 (0.8%)
Ruptured uterus	2	2§ (100.0%)	0 (0.0%)
Others	35	0	0
Total	362	16 (4.4%)	5 (1.4%)

*1, Advanced nephritis, 3-pound fetus; 2, advanced nephritis, 2-pound fetus; 3, eclampsia and nephritis, 3-pound fetus; 4, severe pre-eclampsia, 2¼-pound fetus; 5, recurrent toxemia, nephritis, 5-pound fetus.

†1, Ablatio placentae, 4-pound fetus; 2, ablatio placentae, 4.1-pound fetus; 3, placenta previa, malformation, 6-pound fetus; 4, ablatio placentae, stillborn macerated fetus, 6½ pounds.

‡1, Unable to resuscitate, cause unknown after autopsy, 9¾ pounds; 2, atelectasis, 6¾-pound fetus; 3, cerebral hemorrhage, test of labor, 8¾-pound fetus; 4, died on third day, cause unknown after autopsy, 9-pound fetus; 5, congenital anomalies, 6-pound fetus.

§1 and 2, Stillborn, not macerated; intrauterine asphyxia.

||Two mothers accounted for twins; all four children survived.

Eight of the 362 mothers delivered by cesarean section succumbed on the day of operation or as late as thirty-three days following delivery and must, therefore, be considered maternal deaths, that is, a gross mortality of 2.2 per cent. These have already been mentioned in connection with anesthetics used, but are, herewith, summarized for further discussion.

CASE 1.—This patient was a 30-year-old para o gravida iv with hypothyroidism who had had two early spontaneous abortions followed by a cesarean section because of pelvic dystocia and resulting in delivery of a stillborn child with atelectasis. The fourth pregnancy was terminated under gas-ether anesthesia by cesarean section done primarily because of a twin pregnancy after a former cesarean section. Death was due to shock and occurred three hours after delivery of large twins. Autopsy revealed no further information.

CASE 2.—An 18-year-old primipara had been hospitalized because of high fever, up to 107° F., due to cavernous sinus thrombosis. When moribund and near term, in order to salvage the fetus, elective cesarean section was done under local infiltration anesthesia. A 6-pound living child was obtained and raised, the mother succumbing to her original infection some few hours later. This death cannot be ascribed to the method of delivery.

CASE 3.—This 39-year-old primipara was planned for elective cesarean section because of cephalopelvic disproportion. However, she had a premonition that she would not survive the delivery and remained at home

preparing her will, etc., until after twelve hours of labor. On entering the hospital, the cervix was fully dilated and head overriding the symphysis pubis, so a low cervical cesarean section was done under gas-ether anesthesia. A 9 $\frac{1}{8}$ -pound child was delivered in good condition but the mother died of shock about four hours after operation, in spite of transfusion and other combative measures.

CASE 4.—A 25-year-old primipara was admitted because of severe heart disease. She was delivered before term because of a superimposed toxemia and breech position of the fetus. Spinal procaine was used for the anesthetic. The baby weighed 5 pounds and survived, but the mother succumbed after twenty-four days, the autopsy proving advanced myocarditis. While this is certainly a maternal death, the major operative delivery can hardly be blamed for the unfortunate outcome.

CASE 5.—This 39-year-old multipara was seen for the first time in the third trimester of pregnancy. She had chronic nephritis and was hospitalized and treated for seventeen days in the hope of obtaining a viable fetus. Under observation, her toxemia grew worse and blood pressure eventually reached 284/140. Delivery was under spinal anesthesia and a 3 $\frac{3}{4}$ -pound child was obtained and raised, but the mother died of cerebral hemorrhage twenty-seven days later. In retrospect it seems certain that this mother was sacrificed in waiting for fetal development. However, in view of the advancement of her disease, delivery immediately after hospitalization probably would not have added much to her life expectancy. Certainly this maternal death cannot be said to have been due to the method of delivery.

CASE 6.—In this case, elective cesarean section was done in the thirty-seventh week of gestation on a primipara because she was not expected to live as long as her estimated date of confinement. A 6-pound child was delivered in good condition, but the mother did not succumb to her disease, melanosarcoma with generalized metastases, until thirty-three days later. The operative procedure here had no direct bearing upon the fatal outcome.

CASE 7.—This elderly primipara had multiple myomata uteri and cephalopelvic disproportion as well as asthma. Cyclopropane was the anesthetic employed, and death occurred on the third day due to pneumonia. This maternal death probably could have been avoided by a more judicious choice of local infiltration anesthesia.

CASE 8.—In this instance, low cervical cesarean section was performed late in labor with pelvic dystocia as the indication. However, the patient had no intrapartum fever nor any marked febrile reaction in the immediate puerperium. Nevertheless, her internist administered a large dose of sulfathiazole intravenously on the third day. It must be recorded that she was known to have exhibited sensitivity to another sulfonamide some few months before. She responded with a sharp febrile reaction, temperature to 107° F., convulsions and complete anuria, resulting in death less than fourteen hours later. The chronology of events following the onset of chemotherapy and the previously exhibited sensitivity to it leave no doubt that death was due to this therapy and not primarily to obstetric causes.

As indicated above, these eight maternal deaths following 362 cesarean sections represent an uncorrected maternal mortality of 2.2 per cent. If

we may be allowed to absolve the delivery of all responsibility for death in the patients in Cases 2, 4, 5, 6, and 8, a corrected maternal mortality of 0.83 per cent may be claimed. These figures compare favorably with those reported in other series. With the bearing in mind of these and other possible errors in judgment and with further accumulation of experience with cesarean section.

It is believed that the type of anesthesia for the mother and a higher regard for the life of the baby in the severe toxemia cases offer the best chance of future improvement of the cesarean section problem.

Summary

1. A brief history of the handling of cesarean section cases in Houston, Texas, is given with an analysis of twenty-two years' experience.

2. The incidence of cesarean section in private practice limited to obstetrics was found to be 6 per cent. Reasons for this relatively high rate are given.

3. Morbidity and mortality figures obtained by obstetricians are compared with those obtained by well-recognized general surgeons and by general practitioners.

4. Nitrous oxide-ether anesthesia was the anesthetic of choice, but maternal and fetal mortality rates for all types of anesthetics used are given.

5. The low cervical type outnumbered all other varieties performed in this series by 2.5 to 1.

6. Pelvic dystocia was the primary indication for cesarean section in the great majority of the 362 operations. Maternal and fetal mortality rates associated with each indication are tabulated.

7. Survival rates are tabulated against birth weights of the infants in the toxemia group, and it is concluded that one is hardly justified in performing cesarean section in the interest of the child if it weighs less than 3 pounds but that there is a definite place for cesarean section in salvaging children from mothers with toxemia if the fetus weighs from 3 to 4 pounds or more.

8. Fetal mortality is also tabulated against the primary indication for cesarean section and important conclusions are drawn from these.

9. The gross fetal mortality for the current series was found to be 4.4 per cent and the corrected rate, 1.4 per cent.

10. Brief summaries of maternal deaths are recorded.

11. The gross maternal mortality rate in this series is 2.2 per cent, while the corrected rate is 0.83 per cent.

References

1. Williams, J. Whitridge: A Critical Analysis of Twenty-one Years' Experience with Cesarean Section, *Bull. Johns Hopkins Hosp.* 32: 173-184, 1921.
2. Sanger, Max: *Der Kaiserschnitt bei Uterus-myomen*, Leipzig, 1882.
3. Davis, Neale: Cesarean Section, the Procedure of Choice, *Texas State J. Med.* 24: 883, 1929.
4. Williams, J. Whitridge: The Sloane Hospital for Women; Its Development, Significance, and Possibilities, *AM. J. OBST. & GYNEC.* 17: 795-806, 1929.
5. Johnston, R. A., and Smith, F. B.: Cesarean Section in Houston, Texas; a Statistical Study, *South. M. J.* 24: 725-728, 1931.
6. Bloxson, A. P.: Difficulty in Respiration Seen in Infants Delivered by Cesarean Section, *J. Pediat.* 20: 215-222, 1942.
7. Monahan, C. P., Connally, H. F., and Eastman, N. J.: Experience of Johns Hopkins Hospital With Cesarean Section, *AM. J. OBST. & GYNEC.* 44: 999-1009, 1942.
8. Beecher, H. K.: An Appraisal of Cyclopropane—Editorial, *Surg., Gynec. & Obst.* 75: 797-799, 1942.
9. Belinkoff, S.: Cyclopropane-Pituitrin Incompatibility, *AM. J. OBST. & GYNEC.* 48: 109-113, 1944.
10. Cosgrove, S. A., and Norton, J. F.: Cesarean Section, *J. A. M. A.* 118: 201-204, 1942.
11. Schumann, E. A.: Evaluation of Types of Section and Their Indications, *Am. J. Surg.* 59: 50-59, 1943.
12. Falls, Fred. H.: Mortality, Early and Late, Following Cesarean Section, *J. A. M. A.* 118: 204-209, 1942.
13. Stander, H. J., and Douglas, R. G.: Infantile Mortality Bacteriologic Investigation of Effect of Prolonged Labor on Baby, *AM. J. OBST. & GYNEC.* 46: 1-19, 1943.
14. Kellogg, S. F.: Has X-ray Pelvimetry Reduced the Incidence of Cesarean Section for Cephalo-Pelvic Disproportion, *M. Rec. & Ann., Houston*, Sept., 1942.
15. Greenhill, J. P.: The Increased Incidence of Fetal Abnormalities in Cases of Placenta Previa, *AM. J. OBST. & GYNEC.* 37: 624, 1939.
16. Irving, F. C.: The Conservative Treatment of Premature Separation of the Normally Implanted Placenta, *AM. J. OBST. & GYNEC.* 34: 881, 1937.
17. Cosgrove, S. A., and Conway, D. F.: Premature Separation of the Placenta, *J. Missouri M. A.* 38: 334-340, 1941.
18. Lull, C. B., and Ullery, J. C.: Cesarean Section Under Continuous Caudal Analgesia, *AM. J. OBST. & GYNEC.* 48: 235-240, 1944.

Discussion

DR. LOUIS E. PHANEUF, BOSTON, MASS.—The incidence of 6 per cent or 1 cesarean section in 16.5 cases of Dr. Johnston's series is explained on the basis of repeated cesarean sections and on the reference of complicated cases by other practitioners, thus placing the large number of operations in the hands of one specialist. Emphasis is placed on the fact that "the ultimate well-being of the patient depends less on the surgical skill of the operator than on the obstetric judgment he displayed before picking up his scalpel," a statement with which I believe every specialist in obstetrics would agree.

As to the type of operation performed in this series, there were more than twice as many low or cervical cesarean sections as there were classical cesarean sections. From the standpoint of convalescence and postoperative adhesions, it was noted that the former operation was superior to the latter, this being in keeping with similar observations made by other operators.

The table on anesthesia shows that six different agents were employed. I personally have never seen a cesarean section performed under chloroform anesthesia. Dr. Johnston reports twenty-three deliveries under spinal anesthesia, with two maternal deaths, neither of which could be attributed to the anesthesia, since one woman lived twenty-four and the other twenty-seven days. It is stated that spinal anesthesia is not absolutely free from danger. It is for this reason that I personally refrain from using it. For cesarean section I use two types of

anesthesia: (1) rectal avertin, 70 mg. per kilogram, followed by nitrous oxide-oxygen, with a small amount of ether for relaxation; and (2) local infiltration anesthesia when general anesthesia is contraindicated. As stated by Dr. Johnston, local anesthesia is well adapted to the classical cesarean section; it is also applicable to the low or cervical cesarean section with but little increased difficulties.

The absence of extraperitoneal cesarean section in this group of cases is noted. Dr. Johnston states: "No doubt there have been some indications for such a type of operation, but only during the past year has the technical difficulty of the operation been surmounted." I cannot entirely subscribe to this statement since W. Latzko had proposed his operation in 1908 and in 1938 E. G. Waters revived the Physick-Sellheim operation in America. The gross maternal mortality rate in this review of 362 cesarean sections is 2.2 per cent corrected to 0.80 per cent. This compares favorably with other series of equal numbers. Likewise, the gross fetal mortality of 4.4 per cent corrected to 1.4 per cent is within reasonable limits.

In closing, I would like to emphasize a statement which I had made on several occasions and which was published in 1940; namely, "Careful prenatal study, the use of x-ray pelvimetry, recently developed, examination before labor, under anesthesia if necessary, a test of labor under aseptic conditions, followed by the low or cervical operation when indicated, the use of vaginal antiseptics added to a rigid aseptic technique, and limiting the operation to strict indications will all help in keeping morbidity and mortality in cesarean section at the lowest possible figure."

DR. E. L. KING, NEW ORLEANS, LA.—Most of us will agree with the speaker that the low cervical section is the technique of choice. It is the one we have employed in New Orleans. I agree with him that cyclopropane is not a good anesthetic. I am afraid of its effect on the heart. I prefer ethylene. I have had a few cases with spinal anesthesia but am not in favor of it as a routine.

Two of the sections were done on patients that were hopelessly ill in order to save the babies. That is a situation that is not mentioned in the literature or textbooks, but I think it is a worth-while indication. We have done three such cases at the Charity Hospital in the last twelve or fifteen years. One was a case of cerebral hemorrhage in the mother, another, the case of a woman dying with cerebrospinal reaction to salvarsan.

The question of sections in toxemias will always be a topic for a difference of opinion. In our work we have not done sections for toxemia of pregnancy in a long time, particularly in the convulsive type. We may have done an occasional one for toxemia of the nonconvulsive type, especially in the nephritic group.

Upon another point I would differ with Dr. Johnston and that is the inclusion of the sulfonamide death in the nonobstetric group. Of course, that is not strictly speaking, an obstetric death, but it is a death following cesarean section, apparently caused by the administration of a drug to which the patient was known to be susceptible. I think that we would have to say that that death should be charged either directly or indirectly to the operation.

DR. FREDERICK H. FALLS, CHICAGO, ILL.—The actual incidence of cesarean section depends on who is doing the sections and the circumstances under which he is working. In a community such as Dr. Johnston is working in naturally the men who are getting bad results turn to a specialist in obstetrics for help to improve the results.

There are many men who will not do a cesarean section when it should be done. Even when they get bad results from overconservatism they pat themselves on the back because they are conservative obstetricians. In other words, we may say there are too many cesarean sections being done in the United States, and also that there are too few being done.

As to the question of the low cervical and the classical section, I will agree in part with what he said. Yet I doubt whether in the hands of Dr. Johnston, had he alternated cases, that there would be very much difference in the results of the two operations. I have done every other case for the last ten years by the low cesarean and by the classical methods, respectively, and I cannot see much difference in the results, either in adhesions or postoperative pain. In analyzing the amount of morphine that was given the woman after the operation, it turned out that the ones who had the classical operation needed $\frac{1}{12}$ gr. less than those that had the low cervical.

So far as toxemia is concerned, Dr. Johnston has operated upon these patients and they do not die. I have done the same thing. It is true that good results can be obtained without operation too. I agree also with Dr. Johnston that the x-ray has been disappointing in its value in determining whether or not to use operative procedures.

DR. CLIFFORD B. LULL, PHILADELPHIA, PA.—I do not believe that any man who is practicing only obstetrics should be ashamed of a cesarean incidence of 6 per cent. I was amazed several years ago to find that my incidence was 10 per cent in 1,000 deliveries.

We have just completed a series of 140 cases under fractional spinal and 180 cases under continuous caudal without a death, and I feel strongly that the selection of the anesthetic is very important in doing a cesarean. I also feel very strongly that we are getting away from the use of inhalation anesthesia and will adopt the anatomic approach.

We have not had the opportunity of operating on many patients with toxemia, but in the last two years we have had several cases of eclampsia where we have controlled the convulsions by the use of continuous caudal analgesia and delivered the patient under the same analgesia. We are not prepared to state that we think this will be a treatment for eclampsia, but you can control the blood pressure and the pains.

DR. SAMUEL A. COSGROVE, JERSEY CITY, N. J.—Like the other discussors, I feel that Dr. Johnston's incidence of cesarean section is most moderate in consideration of the conditions of his practice. I agree with Dr. Phaneuf and Dr. King that cesarean section is unwise in the presence of active convulsions; in the other group of toxemic cases to whom Dr. Johnston has applied cesarean section, I think it is not only justifiable but represents the best type of practice.

In the progressive cases of toxemia not responding to proper management there is extreme hazard to the mother, not only immediate but remote, depending on the length of time that that severe toxemia is permitted to persist before pregnancy is terminated. Therefore the time factor becomes important in these cases for the protection of the mother. The known susceptibility of these women to infection, particularly if vaginal interference of any mechanical sort has to be resorted to to terminate the pregnancy, makes cesarean section in many, many instances a most conservative approach.

From the standpoint of the babies, Dr. Johnston's results in the survival of a high proportion of the premature babies certainly justifies his management of these toxemias. A baby inside of a sick mother is a sick baby and the chance of ultimate survival of babies of toxic mothers is not, as a rule, enhanced by prolonged intrauterine existence in the presence of fulminating toxemia.

DR. WILLIAM T. McCONNELL, LOUISVILLE, KY.—On the subject of toxemia, when it becomes apparent that the pregnancy must be terminated in the interest of saving the life of the mother, it is a good thing to investigate the condition of the cervix. Very often this is the determining factor as to whether the patient should be sectioned or delivered from below. To try to bring a premature baby

through an unripe cervix will often cause fetal death, whereas a clean cesarean should be the operation of choice, and would be less shock than a long hard labor to this very sick mother.

DR. J. P. GREENHILL, CHICAGO, ILL.—There are two highlights in Dr. Johnston's paper and in the discussions. The first deals with the type of cesarean operation. I firmly advocate the low cervical operation. I have now done 304 of these operations, with one death. The second point concerns anesthesia. I am a strong advocate of direct infiltration anesthesia because it is the safest of all anesthetics. It is my opinion that spinal anesthesia is the most dangerous anesthetic for pregnant women.

DR. COSGROVE.—I feel that anything I can say about spinal anesthesia is rather insignificant in the light of what is going on in the Philadelphia Lying-in Hospital with continuous caudal and fractional spinal anesthesia. I have no quarrel with local anesthesia. I do not care what you use, provided you do not "knock out" the whole brain by a poisonous agent but restrict the effect of that poison to the lower neurons.

It is true that Dr. Norton showed five anesthetic deaths from spinal anesthesia, or at least coincident with its use, in his series of mortalities. That, as some one here has already pointed out, is meaningless except as related to the total number of such anesthetics.

Dr. Johnston's presentation showed a satisfactory correction for the two deaths in his series which followed spinal anesthesia. And, *mirabile dictu*, we are getting tremendous support just now from Philadelphia, the stronghold of opposition to spinal anesthesia through the eighteen years that we have been using it. There has been, I am sure, tremendous prejudice against spinal anesthesia, and I am also sure that the vast majority of unfortunate results have been due to inexperience, ineptness, and improper technique in its use.

DR. HARVEY B. MATTHEWS, BROOKLYN, N. Y.—I have always been afraid of single injection spinal anesthesia. During my association with the late Dr. Polak, some twenty years ago, we had two deaths from its use. It will be said that we did not know the technique. That might well be because it was new with us at that time. Today, with fractional spinal, I think we have a very safe method of anesthesia. It is easier to administer than local infiltration, less time consuming, and certainly gives a satisfactory anesthesia. It requires a well-trained anesthetist. It is safe for the most severe heart case. Caudal anesthesia may be another answer, but I think fractional spinal given by an expert is easier, safer, and a better anesthetic than caudal.

The decision as to type of operation, classical against low flap or extraperitoneal, is most important. To us the classical operation is all but obsolete. I do not see any necessity at any time, except perhaps where time is an important element, in doing a classical cesarean. We have statistics proving that in the average man's hands the classical operation causes more morbidity and mortality than the double low flap method. I have never reopened the abdomen after a classical section without encountering adhesions, frequently involving some portion of the intestinal tract. Contrariwise, I cannot remember a single case of low double flap or extraperitoneal section in which there were any adhesions worthy of mention.

Dr. Johnston is to be congratulated on his low fetal mortality because fetal mortality in cesarean section still runs from 3 to 10 per cent and higher. It should be impressed upon all those who perform cesarean section, or who have general surgeons do sections for them, that the mere performance of section does not guarantee the life of the baby. The lay public has been all too often misled in this regard.

DR. CHARLES O. McCORMICK, INDIANAPOLIS, IND.—In our clinic we have performed twenty-six sections under pentothal with very satisfactory results. There were no maternal deaths, but one baby was lost. However, this death was not attributable to the use of the anesthetic.

DR. JOHNSTON (closing).—I heartily concur with Dr. McConnell that the condition of the cervix is most important. In the patient with severe toxemia, when interference becomes necessary, a premature infant does not, as a rule, pass through the birth canal without the probability of a considerable hazard to itself. The bad results attributed to cesarean sections in the treatment of patients with eclampsia, as reported by Jeff Miller many years ago, no doubt was due, to a great extent, to the type of anesthetic employed and not to the operative procedure.

A remark of Dr. Falls has influenced me a number of times in dealing with the severe pre-eclamptic cases. Often one is confronted with an infant weighing approximately 4 pounds in breech presentation and the pre-eclampsia continues to become worse in spite of the usual accepted treatment. In such a case Dr. Falls remarked that one should not let the subluxation of one's wishbone press on one's backbone. I am pleased to learn that many agree with me in believing that the future improvement in our cesarean section results will depend on the type of anesthetic agent used and the employment of well-trained anesthetists in all obstetric procedures. In my experience the bad results may have been avoided if a wiser choice in the selection of the anesthetic had been made.

PROLAPSE OF THE URETHRA TREATED BY THE HEPBURN OPERATION*

JAMES R. MILLER, M.D., HARTFORD, CONN.

(From the Hartford Hospital)

THE purpose of this paper is to bring to the attention of gynecologists the simple and useful procedure for the cure of the prolapse of the female urethra which was proposed by Hepburn in 1920 and described again by him in 1927 but which has failed so far to win for itself its merited place among the commonly accepted procedures in our specialty.

The first case treated by Hepburn was that of a 5-year-old child in whom the prolapse had come about after a severe attack of coughing. He regarded the etiology as identical to that of hernia in other places and considered it a partial hernia of the urethra and bladder due to congenitally poor structures. In his presentation of 1927 he reported performing the operation on two adults with excellent results. He described his original technique as follows:

Fill the bladder. Make a suprapubic incision. Put a suture in the bladder so it can be used as a retractor. Work the finger down in the prevesical space under the arch of the pubis. When the neck of the bladder and urethra are freed up enough, draw on the bladder traction suture. The prolapse will be seen to disappear as soon as this traction is made. Then with a curved needle and No. 2 chromic catgut, anchor the neck of the bladder to the periosteum of the pubic arch. Be sure that retraction and anchoring are sufficient so that downward pressure with the hand on the full bladder does not produce any sign of prolapse. Drain prevesical space, if deemed necessary, for twenty-four hours.

Case Reports

Three additional cases have been done by the originator with good results.

CASE 1.—A. D., aged 72, No. 339-959. My first experience with prolapse of the urethra was in August, 1937, when I encountered it in a woman who for six years had had occasional difficulty retaining urine alternating with incontinence. She gave a history of bleeding and moderate pain about the urethra for the previous two weeks. Six years previously there was an acute attack similar to the present one in which her physician had replaced the prolapse by manual manipulation after which she enjoyed comparative comfort. Discomfort had

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been increasing for the past six months. On examination a mushroom-shaped prolapse of the urethral mucosa 2.5 cm. in diameter with points of black necrosis was present. Under spinal anesthesia this was reduced, as outlined by Hepburn, by traction on the neck of the bladder and pressure simultaneously exerted by an assistant against the prolapsed meatus. Instead of a traction suture, I used an Allis clamp which surrounded the urethra at the bladder neck. Three sutures were placed on each side of the urethra, fastening it to the periosteum of the symphysis, and I then fastened the anterior bladder wall to the posterior wall of the abdomen just above the symphysis. Penrose drains were left on each side of the operative area. Following operation she voided spontaneously and left the hospital in good condition in ten days. One month later she had made an excellent recovery with perfect healing as well as bladder control, but a second-degree prolapse of the uterus was noted and a Gellhorn pessary was inserted and changed at monthly intervals until January, 1939, when a Le Fort repair was done. When last seen in 1943 she reported excellent urinary control and no further trouble of any kind.

CASE 2.—L. B., aged 53, No. 418-537. Chief complaint: frequency, burning, urgency, and inability to start voiding and discomfort on sitting. Prolapse of the urethra 2 cm. in diameter was noted in which the entire ring of the meatus rolled outward. Operation was performed Sept. 25, 1941. Urethral dilators were introduced up to 10 mm., but the prolapse could not be reduced in this manner. The meatus with its inverted mucous membrane lay in a hollow recess about 2 cm. in diameter. The Hepburn suspension operation was then done, reducing the prolapse without difficulty and using two sutures on each side of the urethra, fastening it to the posterior aspect of the symphysis with additional sutures on the anterior surface of the bladder, as previously described. Penrose drains were inserted. At the end of the operation eversion had been completely reduced. The meatus measured 1 cm. in diameter and the urethra was snugly suspended behind the symphysis. She made an afebrile convalescence and required catheterization only once on the first day. The follow-up Oct. 20, 1941, showed the urethra still held high, and her only complaint was that she wet herself when voiding, perhaps due to the funnel-shaped opening of the meatus. Follow-up March 17, 1943: The patient came in for treatment of *Bacillus coli* cystitis which was quickly controlled. The urethra was snugly held and voiding was now normal.

CASE 3.—H. S., aged 57, No. 397-976. Complaint: dysuria for two months. She had been treated in another city for atrophic vaginitis by means of estrogens and the urethra had been "coagulated." For three weeks following this procedure she had bled profusely. Pelvic examination showed a small rectocele and a mushroom-shaped prolapse of the urethra measuring 3 cm. in diameter with markedly reddened mucosa. The suprapubic suspension operation was done. It was noted that the urethra fell away markedly from the symphysis suspended only by a fibrous ligament which I made use of in suspending the urethra to the symphysis. In the region of the internal urethral sphincter, there were large dilated veins. The usual sutures were placed and Penrose drains inserted. At the end of the operation inspection showed that the prolapse had been reduced except for redundancy of the right lateral urethral wall. Follow-up Nov. 9, 1940: Abdominal wall well healed, urethra well suspended except for bulge

of the urethral wall from 6 to 10 o'clock, presenting an appearance at this point similar to that when first seen. Under cocaine this area was coagulated with a flat electrode, using the bipolar current. This patient moved out of town and appeared to be very dissatisfied with the results of the operation and although she was a most difficult person to handle, I am obliged to rate her results as only partially satisfactory. A recent letter from her daughter reports that she is comfortable and that no further treatment has been given.

CASE 4.—M. F., aged 49, No. 486-369. This patient had previously been treated for carcinoma of the cervix stage 2, grade 2, transitional cell type. Intrauterine radium was given totaling 3,000 mgh. and deep x-ray therapy totaling 5,300 r. Regression of the carcinoma was apparently complete at least for one year. When first admitted, a prolapse of the urethra was noted measuring $2\frac{1}{2}$ cm. in diameter with minimal symptoms, though showing a squamous-cell metaplasia of the prolapsed mucosa. Suspension of the urethra was done June 2, 1944, and no difficulty was encountered because of fibrosis due to radiation. At the end of the operation complete disappearance of the prolapse was observed. Follow-up examination ten weeks later showed an incomplete reduction of the prolapse but with adequate and symptomless urinary control. The result is only partially successful, though the prolapse in her case is adequately protected from trauma by the surrounding tissues.

Discussion

Minor increase of prolapse of the urethra in which only one wall of the urethra is everted has been encountered, and our files contain the histories of several patients who were easily cured of a "urethral pile" by simple excision as is done with a hemorrhoid. Several histories also record a marked dilatation of the meatus with prolapse of the posterior wall simulating prolapse of the posterior vaginal wall seen in rectocele. Different operators have found no difficulty in repairing this defect by a miniature "perineorrhaphy" while repairing the cystocele and other elements of a genital prolapse. These minor conditions are not the chief concern of this paper but rather the symmetrical eversion of all the urethral walls.

The usual surgical procedure of circular amputation was also recorded in our files. Though follow-up records are incomplete, it would seem that a minor degree of eversion of the urethra can be repaired by circular excision, though an extensive resection would leave a considerably shortened urethral canal and might even result in incontinence of urine. One girl, a moron aged 8, recovered from repair of inguinal hernia and a circular amputation by cautery of a urethral prolapse. She is living at present without urinary difficulty at the age of 22 years.

The danger attendant upon extensive resection is illustrated by the unfortunate result obtained in a patient whose prolapsed urethra was resected in a neighboring city. Complete incontinence resulted with an aperture, admitting two fingers, which replaced the urethral canal. Hepburn implanted both ureters into the colon with excellent results.

Summary

Prolapse of the female urethra is a relatively rare condition which should be observed most frequently by gynecologists. Circular excision of the prolapsed mucosa in a manner similar to the Whitehead operation for hemorrhoids is discarded in favor of the suprapubic suspension of the urethra and bladder as advocated by Hepburn. This operation is simple, effective, and gives lasting good results and can be performed not only in children, but also in the aged and even in the presence of marked debility.

It seems probable that the angulation of the urethra which is accomplished by this suspension procedure may have a useful place in the treatment of urinary incontinence where the urethra and its voluntary sphincter have broken away from its normal attachments to the supporting fascia near the symphysis.

References

1. Hepburn, T. N.: Prolapse of Female Urethra, *Surg., Gynec. & Obst.* 31: 83, 1920.
2. Hepburn, T. N.: Prolapse of the Urethra in Female Children, *Surg., Gynec. & Obst.* 44: 400, 1927.
3. Miller, J. R.: Cystocele Repair, *New England J. Med.* 220: 61-64, 1939.

179 ALLYN STREET.

Discussion

DR. EMIL NOVAK, BALTIMORE, MD.—Dr. Miller has devoted his paper to an exposition and championship of the Hepburn operation, which I have never performed. I doubt, however, whether this procedure has been practiced by many, or any, of the other Fellows of this Society. The fact that the operation was described twenty-four years ago would suggest that the method has not appealed to most surgeons as preferable to those more commonly employed.

The term prolapse has often in the past been applied to the condition now usually spoken of as urethrocele, in which the urethra sags downward and forward, away from the pubes. More recently, however, the term has come to be used in the sense that Dr. Miller has employed it, but the pathology is not always the same. Often there is only a prolapse or rolling out of the mucosa, much as the lining of a sleeve rolls out when it is too long for the cloth of the sleeve. A better term for such cases would be eversion or ectropion.

Speaking generally, the treatment of prolapsed organs is not to hang them up, but to support them from below, as in the treatment of uterine prolapse. The Hepburn operation seems to me quite comparable to the now discarded and unsatisfactory Murphy sigmoidopexy for the relief of prolapse of the rectum, or to the old-time ventral fixation of the uterus. The urethra is pulled up taut and with the vesical neck is fixed to the symphysis. Aside from the undesirability of thus fixing a normally motile organ, the procedure impresses me as an unnecessarily extensive one, with at least some hazard of wounding the bladder and urethra.

No one sees a great many cases of the marked degrees of urethral prolapse, but over the years I have observed a fairly considerable group. The more moderate degrees offer very little difficulty in management, requiring either no treatment at all or simple and generally satisfactory procedures like cauterization with a fine nasal point (much as we do in cervical erosion) or simple plastic

procedures such as the Kelly-Burnam technique, or some other adapted to the individual situation. Even in the occasional very pronounced case, with perhaps a tumorlike protrusion of a considerable segment of urethral mucosa and at times actual strangulation, my experience with the circumcision type of operation has been very satisfactory and I have not noted incontinence or stricture as sequelae. This is well illustrated in the case of a patient 71 years old. She had borne no children, and the vaginal canal was narrow and contracted. I mention this to emphasize that in most of these cases there is no prolapse of the urethra as a whole, only the mucosa being involved. It would seem illogical to fix such an urethra in the manner prescribed by Hepburn when the condition can be much more simply and safely corrected by approaching it from below. Much, therefore, as I respect Dr. Miller's experience and judgment, I do not feel any great urge to resort to the procedure which he has endorsed.

DR. MILLER (closing).—I agree with Dr. Novak that the minor degrees of prolapse call for no treatment. I emphasized in the paper that this operation dealt only with the more severe types and if we limit its employment to those cases where the prolapse and eversion involves at least one-half of the canal, there is a distinct use for it. The suprapubic operation is extremely easy, rarely takes twenty minutes, and can be done on patients with considerable debility.

Concerning the analogy Dr. Novak has made with prolapse of the uterus and its repair from above, I believe it is not quite correct to compare this operation with ventral fixation of the uterus. For the last several years I have been following a suggestion made by Dr. Meigs, repairing prolapses from above, with excellent results, particularly where an enterocele is a large factor. It is difficult to see how a good suspension can be done as well from below when you see the tissues fall away from the symphysis, as is demonstrated with the exposure from above.

(The Transactions of this meeting will be concluded in the May issue.)

Department of Reviews and Abstracts

Selected Abstracts

Gynecology

Barrett, C. W., and Lash, A. F.: Pelvic Reactions to Infection, *Am. J. Surg.* 64: 45, 1944.

Four hundred and ninety-three cases of pelvic inflammatory disease operated upon at the Cook County Hospital are analyzed, and the authors offer the following conclusions:

1. Although the gonococcus may be the common primary or secondary invader the pyogens play the chief role in permanently destroying the female pelvic organs.
2. Methods of treatment other than surgical are palliative at best.
3. Since the pyogenic organisms are commonly found in the tissues, operation is to be postponed until immunization of the patient has occurred.
4. Temperature, leucocyte curve, and degree of tenderness of the lower abdomen are the best criteria for operation at the present time.
5. Applying the above principles in the series here presented has resulted in a mortality of only 1.42 per cent, the lowest ever reported.
6. A detailed "plan of operation" is recommended which the authors feel is definitely related to the low mortality.

FRANK SPIELMAN.

Scott, G. D., and Scott, I. H.: Extrauterine Fibromyomas, *Am. J. Surg.* 54: 391, 1941.

Three cases of extrauterine pelvic tumor are presented, 2 of which were fibromyomas and the third a fibrosarcoma arising from a fibromyoma. Two of the tumors were found within the right broad ligament and the third was in the anterior vaginal wall below the urethra. The latter was accompanied by marked urinary disturbances. None of the tumors showed any connection with the uterus.

FRANK SPIELMAN.

Extrauterine Pregnancy

Denoon, H. L., Jr., and Henderson, W. C.: Ectopic Pregnancy, *Am. J. Surg.* 63: 257, 1944.

A case of abdominal pregnancy in a 40-year-old colored woman is described. At the time of operation, it had been retained for 8 years and was 8 months in size. It arose from the region of the left broad ligament and was attached to the small intestine in such a fashion as to produce constriction of one of the loops. From the authors' description, it appears to have originated in the left ovary. The membranes were calcified, but not the fetus. It was removed with little difficulty. The literature on the subject is reviewed and other similar cases mentioned.

FRANK SPIELMAN.

Dibbins, S. A.: Abdominal Pregnancy, *Am. J. Surg.* 63: 402, 1944.

This is a report of a remarkable case of abdominal pregnancy. It occurred in a 23-year-old white female, who had had an ectopic pregnancy one year before, for which laparotomy was performed and at which time a uterine suspension was done. During the pregnancy here described, conditions appeared to be normal except for repeated attacks of lower abdominal crampy pain. The fetal heart could be heard and movements felt until just before term. Severe abdominal pain necessitated hospitalization and an x-ray film showed a fetus lying in the transverse position. Abdominal pregnancy was not suspected but cesarean section was decided upon on the basis of the position of the fetus and the patient's condition. The abdomen was opened with difficulty, and in attempting to reach the amniotic sac, the placenta was incised resulting in profuse bleeding. A 9-pound, 4-ounce calcified fetus was removed, and the bleeding controlled first by packing and later by suture through the placenta. Shock was combated by transfusions during and after the operation, and the abdomen closed without drainage. The postoperative course was characterized by sustained temperature, and a steady fall in hemoglobin, so that a second laparotomy was performed 5 weeks after the first operation. At this time the necrotic placenta was found attached to the sigmoid, mesentery, small intestine and uterus, and its removal resulted in a sigmoidal defect which was repaired with silk sutures. Following this operation, a fecal fistula developed which ultimately closed spontaneously. Recovery was also complicated by phlebitis.

FRANK SPIELMAN.

Newborn

Farber, Sidney: The Relation of Pancreatic Achylia to Meconium Ileus, *J. Pediat.* 24: 387, 1944.

The author reports postmortem examination of eighteen infants who presented the clinical picture of high intestinal obstruction caused by meconium, revealed in each instance an obstructive lesion in the pancreas characterized by inspissation of secretions, dilatation of ducts, atrophy of acini and fibrosis of the pancreas. An examination of the material obtained from the duodenum, in a patient who had a typical story of meconium ileus, revealed no evidence of tryptic activity.

Experiments performed back in vitro and in vivo, with the altered meconium in patients with meconium ileus, have shown that this material may be brought into a semifluid or fluid state by the action of dilute solutions of extracts of the pancreas.

The application of these observations to the treatment of patients with meconium ileus has resulted in relief of the intestinal obstruction.

JAMES P. MARR.

Taylor, G. L., and Race, R. R.: Hemolytic Disease of the Newborn Infant, *Brit. M. J.* 4338: 288, 1944.

The authors describe their results with "St" serum which discloses the genotype of half the persons who are homozygous Rh-Rh. This serum agglutinates the blood of all Rh negative rhrh and of all heterozygous Rhrh persons, but it fails to react with about 20 per cent of bloods (St negative) all of which must therefore be homozygous Rh-Rh and represent about half of the Rh positive homozygotes—about 38 per cent of the population. In a random sample of Rh-positive males, about 3 out of 7 must be homozygous, and 4 must be heterozygous. There is a marked preponderance of homozygous fathers in families affected by hemolytic disease of the newborn infant. The homozygote appears to be 4 or 5 times more dangerous than the heterozygote.

WILLIAM BERMAN.

Miscellaneous

Loomis, Frederic: *De Senectute* (Marcus Tullius Cicero), *West. J. Surg.* 52: 175, 1944.

The paper on "Old Age" by Dr. Frederic Loomis read before the Twelfth Annual Meeting of the Pacific Coast Society of Obstetrics and Gynecology is full of the grace and wit which distinguishes the writing of a worthy successor of Dr. Oliver Wendell Holmes. He has dealt with a subject which is of interest to us all, now that the expectation of life is extended. Taking Cicero's discussion—"De Senectute"—with Cato for his text, and a less apposite text from St. Paul's epistle to the Romans he has applied Cicero's apothegms to the problems which confront the retiring doctor: How to take Old Age. Old Age is a term which is very elastic. Sophocles wrote brilliantly when he was almost an octogenarian, and Dr. Robert Bridges, the late poet-laureate of England, published his magnum opus: "The Testament of Beauty," when he was in the eighties.

But we may take it that, when a man is no longer absorbed by his work, he is too old for it and he would be well advised to retire and seek a change of occupation. In most cases this would be a hobby. That Dr. Loomis is well provided in this respect all who read his essay will realize. Without an intellectual pursuit old age falls upon a man prematurely. This is well illustrated by the short time left to members of the police force to enjoy their pensions. Therefore, all the more is it necessary for members of the learned professions to provide themselves with some form of activity which will keep the mind exercised and interest in life continuous and alert.

Men became old, earlier or later, in different periods of history. We are surprised to find Shakespeare speaking of "Old John of Gaunt" when "John" was only fifty. Shakespeare himself died of premature old age at fifty-two. On the other hand, Michelangelo's creative genius lasted until his death at ninety. Neither Cato nor Cicero lived out their lives. Cato committed self-homicide at 85, and Cicero was assassinated at the age of 63.

Dr. Loomis discussed occupations suitable to old age. What to do with yourself. Attend to your garden, was the advice of Voltaire. But as Dr. Edward N. Ewer who opened the discussion on Dr. Loomis' paper pointed out, farming is an occupation rather too trying for an old man. Metchnikoff was willing to await the time when old age became its own answer and a man was content to forget in sleep the *tedium vitae*. But by old age Metchnikoff meant 124 years.

There was an artist in China who devoted all his life to painting a blade of grass. When he was ninety he said that he was nearing perfection, and that when he reached 100 he hoped to achieve it. But this devotee, this amateur, this art-absorbed man never became old. The lesson of Dr. Loomis' excellent paper may be summed up: Keep the mind young and Old Age will be kept at bay.

JAMES P. MARR.

Schauffler, Goodrich C.: *Vagaries and Historical Backgrounds in Obstetrics*, *West. J. Surg.* 52: 182, 1944.

This article opens with an unusual introductory aura—presaging an amusing discussion of the midwives of the Middle Ages. These creatures, more useful than any physician of their century, are lost in the welter of the author's thoughts. No mention is made of Trotula or the Salernitan school, yet her *De passionibus mulierum* represented the best knowledge of the period on the subject of midwifery.

The medical knowledge of Princess Anna Comnena, daughter of Emperor Alexius (1081-1118), was almost professional, and at times it enabled her to grasp truths in advance of the doctrines and beliefs of her day. Louise Bourgeois (1609), who

as midwife to Marie de Medici, ushered in Louis XIII, had been instructed by Paré and Guillemeau. Justine Siegmundin (1690) was probably the first to induce labor by artificial rupture of the membranes. All these the author characterizes as "simply hard-shelled, self-sufficient old harpies with dirty fingernails." Yet, these same midwives showed the way for Semmelweis a century later, only to receive the scorn of Scanzoni.

Deftly, at least the author has drawn analogies between the old barber surgeons and the present-day abortionists, and the radical surgical obstetrician. The analogy is unexplainable.

There are several quotations from Mariceau, and P. Dionis which are well worth reading as an item of history, but of little present-day value.

The author in a humorous vein has singled out the various estrogens, white magots, and snake venoms, and has subjected them to a withering scorn. These, he has compared to the juices of leeks, woman's milk, dissolved swallows' nests, and other absurd therapeutic measures of the ancients, forgetting the esteemable value of so lowly a substance in the scale of things as the ordinary mold-penicillin, or the liver of the cod fish.

Paré, John Maubray, Palmer Findley and E. Novak was satirized for their complacent platitudes. Paré, who reintroduced internal podalic version, version having been lost for a thousand years. John Maubray, an early English author, is singled out for one page of incomprehensible verbiage, overlooking that he antedated both Smellie and Hunter in his knowledge of retroversion of the uterus. Findley and Novak may speak for themselves.

Indeed, an astounding and provocative essay for one who treats his medical history with respect and reverence.

JAMES P. MARR.

Hartman, Carl G.: Origin of Ovarian Adhesions From Organized Liquor Folliculi in the Rhesus Monkey, Surg., Gynec. & Obst. 78: 391, 1944.

Adhesions from the ovary to the omentum or Fallopian tube are described in a series of monkeys operated at The Carnegie Institute, Baltimore, during the course of a study on ovulation and fertilization. The adhesions varied in size from delicate strands to 1 millimeter in diameter. It is the opinion of the author that these adhesions arise from the follicle after the extrusion of the egg. To start with, these consist of strands of the thick, tenacious liquor folliculi of the third order. Eventually, fibrous connective tissue is laid down on the mucous scaffold. Proof of this is based both on the microscopic appearance of the fibers and the fact that many of them can be traced to corpora albicantia.

L. M. HELLMAN.

Items

American Board of Obstetrics and Gynecology

Examinations

The general oral and pathology examinations (Part II) for all candidates will be conducted at Atlantic City, New Jersey, by the entire Board from Wednesday, June 13, through Tuesday, June 19, 1945. The Hotel Shelburne in Atlantic City will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel.

Candidates for *re-examination* in Part II must make written application to the Secretary's Office not later than April 15, 1945.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

Deferment without time penalty under a waiver of our published regulations applying to civilian candidates, will be granted if a candidate in Service finds it impossible to proceed with the examinations of the Board.

Applications are now being received for the 1946 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

Erratum

In the article entitled "Cervical Pregnancy," by W. E. Studdiford, M.D., New York, N. Y., which appeared in the February, 1945, issue of the JOURNAL, the second sentence of the legend to Fig. 2, on page 183, should read: "Further development leads to (1) expansion of cervical mucosa overlying nidation site in direction of cervical canal; or (2) rupture of infra- or supravaginal cervix if the cervical muscularis is deeply invaded by chorion."

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

- American Gynecological Society.** (1876) *President*, Edward A. Schumann, Philadelphia, Pa. *Secretary*, Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** (1888) *President*, Lewis F. Smead, Toledo, Ohio. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.
- Central Association of Obstetricians and Gynecologists.** (1929) *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Dallas, Tex. Annual meeting not announced.
- South Atlantic Association of Obstetricians and Gynecologists.** (1938) *President* Oren Moore, Charlotte, N. C. *Secretary*, T. J. Williams, University, Va. Annual meeting cancelled.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas Tex. Next meeting, Philadelphia, Pa., June 18-22, 1945.
- New York Obstetrical Society.** (1863) *President*, W. E. Studdiford. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** (1868) *President*, Charles A. Behney *Secretary*, John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** (1878) *President*, William J. Dieckmann. *Secretary*, Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** (1890) *President* Chas W. Mueller. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society.** *President*, Edward Friedman. *Secretary*, Carroll J. Fair, Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Charles Hunt. *Secretary-Treasurer*, Karl H. Martzloff, 808 Medical Dental Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** (1934) *President*, H. A. Power. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** (1861) *President*, George Van S. Smith. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.
- New England Obstetrical and Gynecological Society.** (1929) *President*, Roy J. Heffernan, Brookline, Mass. *Secretary*, Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.

*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

- Pacific Coast Obstetrical and Gynecological Society. (1931) *President*, T. Floyd Bell. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society. (1933) *President*, James R. Costello. *Secretary*, Geo. J. Ellis, 1150 Connecticut Ave., N.W., Washington, D. C., Fourth Saturday, October to May.
- New Orleans Obstetrical and Gynecological Society. (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society. (1924) *President*, S. A. Weintraub. *Secretary*, Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society. (1929) *President*, R. Glenn Craig. *Secretary*, D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists. (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Owen C. Foster. *Secretary*, Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Obstetric Society of Syracuse Hospitals. (1938) *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.
- Alabama Association of Obstetricians and Gynecologists. *President*, J. M. Weldon, Mobile, Ala. *Secretary*, Eva F. Dodge, Montgomery, Ala.
- San Antonio Obstetric Society. *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society. (1941) *President*, R. Philip Smith. *Secretary*, Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings held on third Wednesday of each month.
- Denver Obstetrical and Gynecological Society. (1942) *Secretary*, Emmett A. Mechler, 1612 Tremont St., Denver, Colo. Suspended during war.
- Wisconsin Society of Obstetrics and Gynecology. (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society. (1937) *President*, Geo. D. Huff. *Secretary*, D. Dalton Deeds, 2001 Fourth Ave., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology. (1938) *President*, Ralph E. Leigh, Grand Forks. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society. (1936) *President*, A. L. Carson, Jr. *Secretary*, L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.
- Columbus Obstetrical and Gynecological Society. (1944) *President*, Zeph J. R. Hollenbeck. *Secretary*, Wynne M. Silbernagel, 9 Buttles Ave., Columbus Ohio. Meetings held last Wednesday of each month.
- Nassau Obstetrical Society. (1944) *President*, Arthur C. Martin. *Secretary*, William S. C. Dolan, 2870 Northern Blvd., Manhasset, N. Y. Meetings, bi-monthly from October to May.
- Bronx Gynecological and Obstetrical Society. (1924) *President*, Jacob Clahr. *Secretary-Treasurer*, J. Irving Kushner, 1840 Grand Concourse, New York, N. Y. Meetings, fourth Monday monthly from October to May.

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American Association of Obstetricians, Gynecologists,
and Abdominal Surgeons

Fifty-Sixth Annual Meeting, Sept. 7 to 9, 1944

(Concluded)

TOTAL ABDOMINAL HYSTERECTOMY

Observations Based on a Series of 1,925 Patients*

WILLIAM F. MENGERT, M.D., DALLAS, TEXAS, AND

RODNEY STOLTZ, M.D., IOWA CITY, IOWA

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BETWEEN Jan. 1, 1926, and Dec. 31, 1943, 2,820 women underwent some form of hysterectomy at the University of Iowa. In the early years of the present administration of the Department of Obstetrics and Gynecology, subtotal hysterectomy was performed routinely with the total operation reserved for necessity. During 1932, the clinic policy changed; more and more total hysterectomies were elected so that during the next two years, 1933 and 1934, not a single subtotal operation was done. This rigorous policy was relaxed for the next few years, but since 1938 more than 90 per cent and since 1940 more than 95 per cent of all abdominal hysterectomies have included the cervix.

The 2,820 operations included 1,925 total, 393 subtotal, 475 vaginal, and 27 radical (Wertheim) hysterectomies; the year by year distribution is shown in Fig. 1. The purpose of this paper is to detail the experience obtained in performing the 1,925 total abdominal hysterectomies.

The Patient

The women of the series were preponderantly white (94.9 per cent), mostly indigent, and ranged in age from 20 to more than 70 years, with an average of 50 years. Their weights ranged from less than 100 to more than 250 pounds, with an average of 130. Forty per cent

*Read at the Fifty-sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1944.

had never undergone an abdominal or vaginal operation. Only 326, or 16.9 per cent, were nulliparous, the remainder having had an average of four pregnancies.

Preoperative Course

Fifty-nine per cent of the patients remained in the hospital from two to five days prior to operation, and 27 per cent remained more than six days. Operation within twenty-four hours following admission took place in only 12 per cent. The most common preoperative complications were hypertension and anemia, occurring in 493 and 407 women, respectively, and in association with each other eighty-four times. Fourteen patients suffered from diabetes mellitus and twelve were febrile.

It has always been customary to examine all patients at a group session and only rarely did a patient escape examination by the chief or one of his associates. The accuracy of these preoperative diagnoses was 71.9 per cent. For the sake of greater accuracy, postoperative rather than preoperative diagnoses (Table I) are tabulated. Malignant tumors of the uterus (167) or of the ovary (67) were present 234 times. Since no one would question the necessity of performing total hysterectomy in these conditions, it is obvious that removal of the cervix was demanded in 12.1 per cent, or in 1 patient in 8.

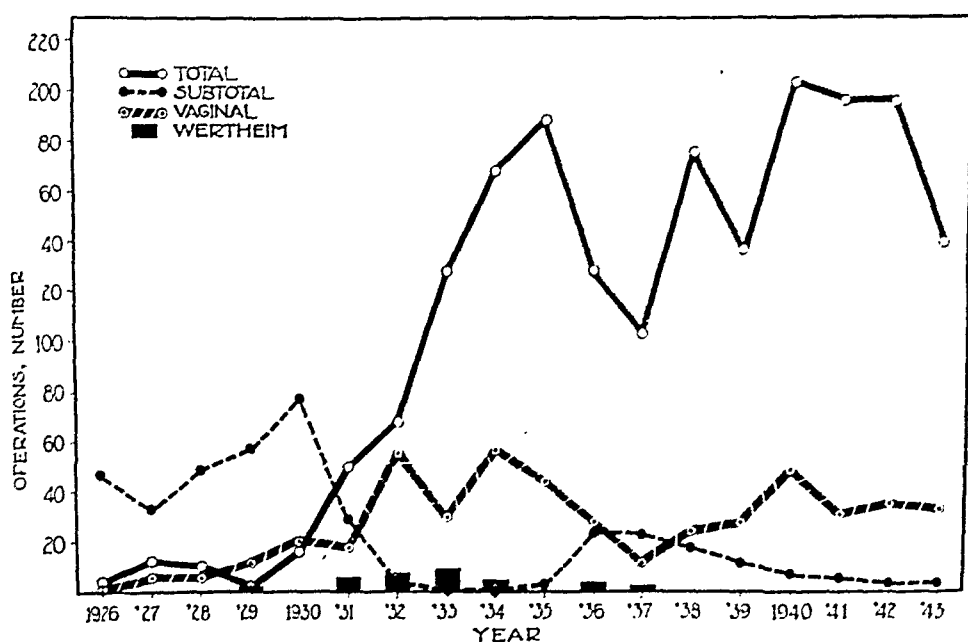


Fig. 1.—Annual incidence of types of hysterectomy.

The Operator

Five senior staff members performed 36 per cent, eighteen senior residents, with assistants usually of lower rank, 39 per cent, and assistant or associate residents, generally assisted by more experienced operators, 475 operations, or 25 per cent. The mortality rates for these three groups, senior staff, senior residents, and others, were 2.9, 2.0, and 0.6 per cent, respectively. This difference is to be expected, since difficult technical procedures and poor risk patients were generally assigned to experienced operators.

The Operation

Since the techniques involved in total hysterectomy will be reported elsewhere, they will be omitted here. Suffice it to say that the vaginal apex was closed or left open, more often the latter, and that no attempt was made in any way to support the vagina with the round, ovarian, or infundibulopelvic ligaments. (Figs. 2-6.)

TABLE I. DIAGNOSES AS DETERMINED DURING AND FOLLOWING OPERATION

	NUMBER OF PATIENTS		
	SOLE FINDING	ASSOCIATED WITH OTHER LESIONS	TOTAL
Fibromyoma of the uterus	616	240	856
Benign ovarian tumor		64	
Pelvic inflammatory disease		55	
Malignant uterine tumor		10	
Miscellaneous		111	
Functional bleeding	247	125	372
Fibromyoma of uterus		45	
Benign ovarian tumor		30	
Miscellaneous		50	
Pelvic inflammatory disease	172	157	329
Fibromyoma of uterus		55	
Functional bleeding		31	
Benign ovarian tumor		30	
Miscellaneous		41	
Benign ovarian tumor	150	168	318
Fibromyoma of uterus		64	
Pelvic inflammatory disease		30	
Functional bleeding		21	
Miscellaneous		53	
Malignant uterine tumor	133	34	167
Fibromyoma of uterus		10	
Miscellaneous		24	
Malignant ovarian tumor	48	19	67
Miscellaneous		19	
Miscellaneous diagnoses	74	141	215

Because of multiplicity of lesions, totals are more than 1,925.

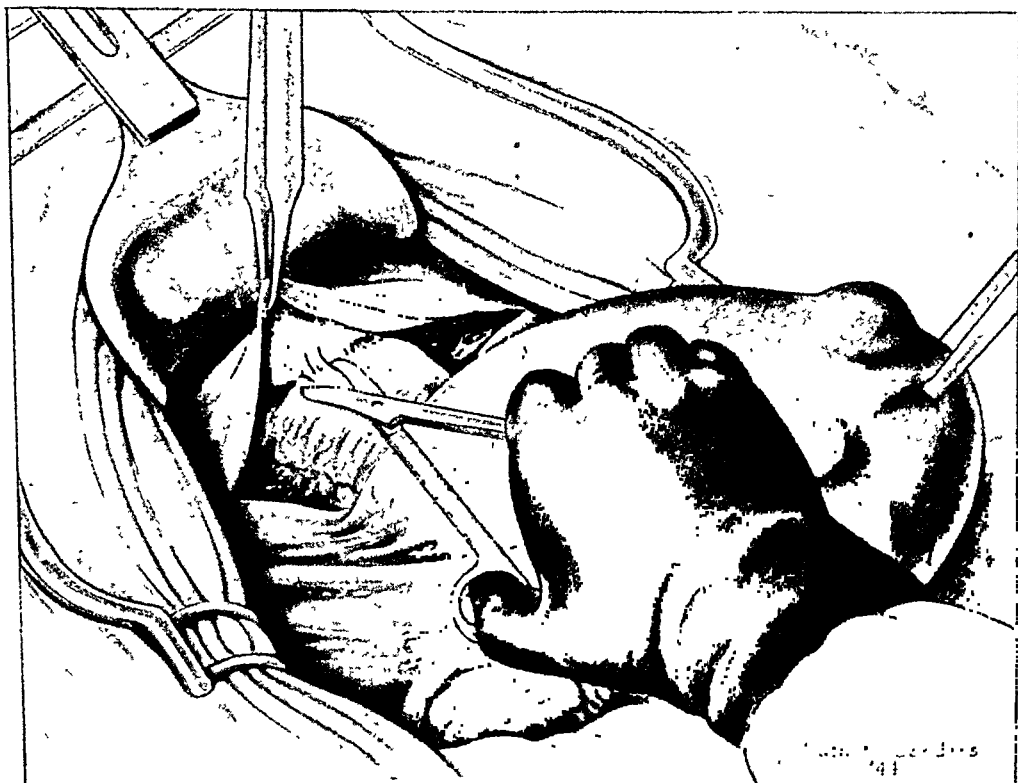


Fig. 2.—Technique of total abdominal hysterectomy—downward dissection of the bladder. The bladder is lifted up with forceps and the cleavage line developed with scissors by a cutting and pushing motion.

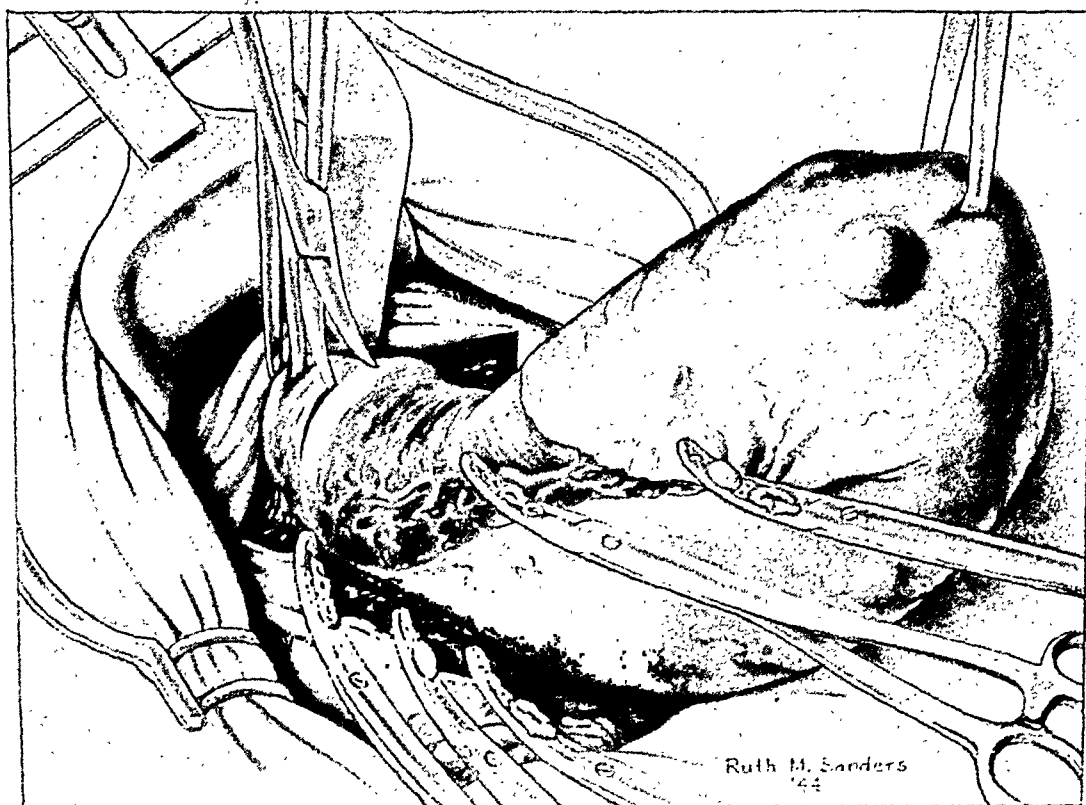


Fig. 3.—Technique of total abdominal hysterectomy. The vagina is opened anteriorly just below the cervix. After opening, a fluffed sponge is tucked into the vagina to absorb fluid left from preoperative vaginal preparation.

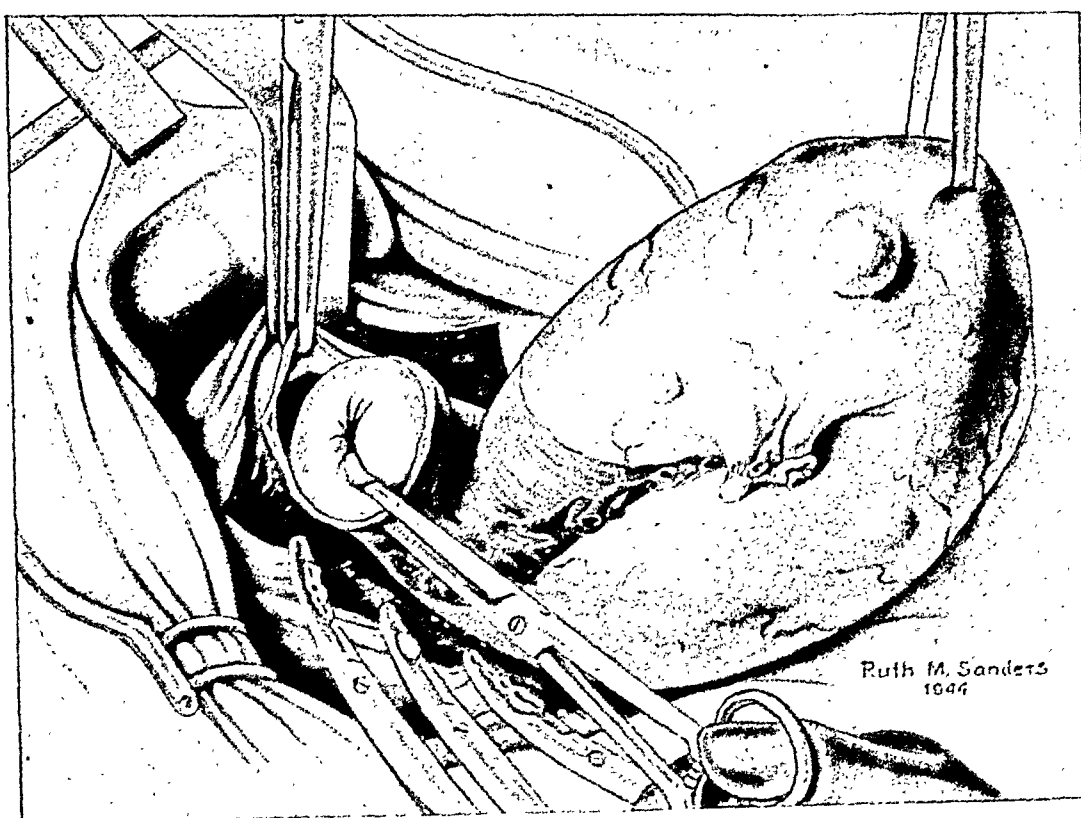


Fig. 4.—Technique of total abdominal hysterectomy. The cervix is retracted with a volsellum forceps and the vagina circumscribed under direct vision and as close to the cervix as possible. No special attention is paid to the sacrouterine ligaments although they may be clamped if desired.

TABLE II. ELECTIVE OPERATIONS COMBINED WITH TOTAL HYSTERECTOMY

	NUMBER OF PATIENTS
Bilateral salpingectomy	767
Bilateral oophorectomy	716
Appendectomy	704
Unilateral oophorectomy	583
Unilateral salpingectomy	496
Dilatation and curettage	150
Vaginal plastic repair	84
Herniorrhaphy	54
Miscellaneous	64

Since associated elective operations were frequently multiple, the total is more than 1,925.

Associated elective operations are detailed in Table II and the anesthetics employed are listed in Table III. In no instance was a patient operated upon without anesthesia. During 1943 and the latter part of 1942, injections of a purified extract of curare^{*} were successfully employed with cyclopropane and ethylene anesthesia to relax the abdominal musculature.

Complications, usually of a technical nature, were experienced in 1,013, 53 per cent, of the patients (listed in Table IV) and by and large were relatively minor. On the other hand, it may be significant that twenty-three of the thirty-eight fatalities were recruited from the group of patients with operative complications. Stated differently, this death rate was 2.3 as compared with 1.6 per cent in the uncomplicated group.

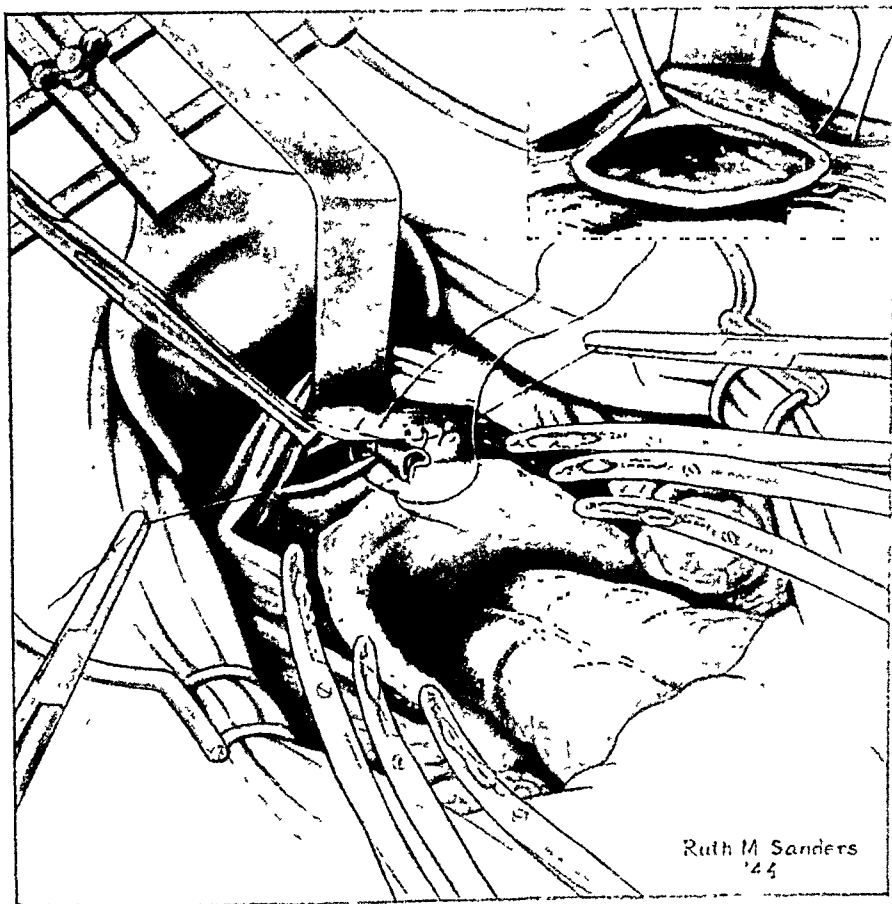


Fig. 5.—Technique of abdominal hysterectomy. The vagina is closed with a continuous whipstitch of chromic 1 catgut, which includes the whole thickness of vaginal mucosa and the fascia propria of both the anterior and posterior walls. Since the sacrouterine ligaments are part of the posterior fascia propria, they are included in this suture. A soft rubber drain, removed the next morning, is left in situ to provide vaginal drainage for any bleeding. Optionally, the vagina may be left wide open. In this event, the edges must be whipped over with interrupted or continuous sutures in order to effect hemostasis of the vaginal cuff. Note that the round and ovarian ligaments are not sutured to the vaginal cuff.

Inset: Since vaginal branches of the uterine artery sometimes produce troublesome postoperative bleeding, mattress sutures are placed bilaterally.

*Intocostrin (Squibb).

TABLE III. THE ANESTHETIC

	NUMBER OF TIMES EMPLOYED.		
	TOTAL	ALONE	IN COMBINATION
Ether	1188	68	1120
Ethylene	755	56	699
Nitrous oxide	482	2	480
Spinal	464	286	178
Cyclopropane	391	269	122
Local infiltration	7	1	6
Other	11	11	0

Because of multiple combinations of anesthetics, the sum of column 1 is more than 1,925.

One anesthetic was employed in 693 patients, two in 1,087, three in 144, and four in 1. This total equals 1,925.

TABLE IV. COMPLICATIONS DURING OPERATION

	TIMES NOTED
Troublesome adhesions	833
Troublesome bleeding	115
Shock	54
Large bowel injury	12
Ureteral ligation or division	10
Bladder injury	12

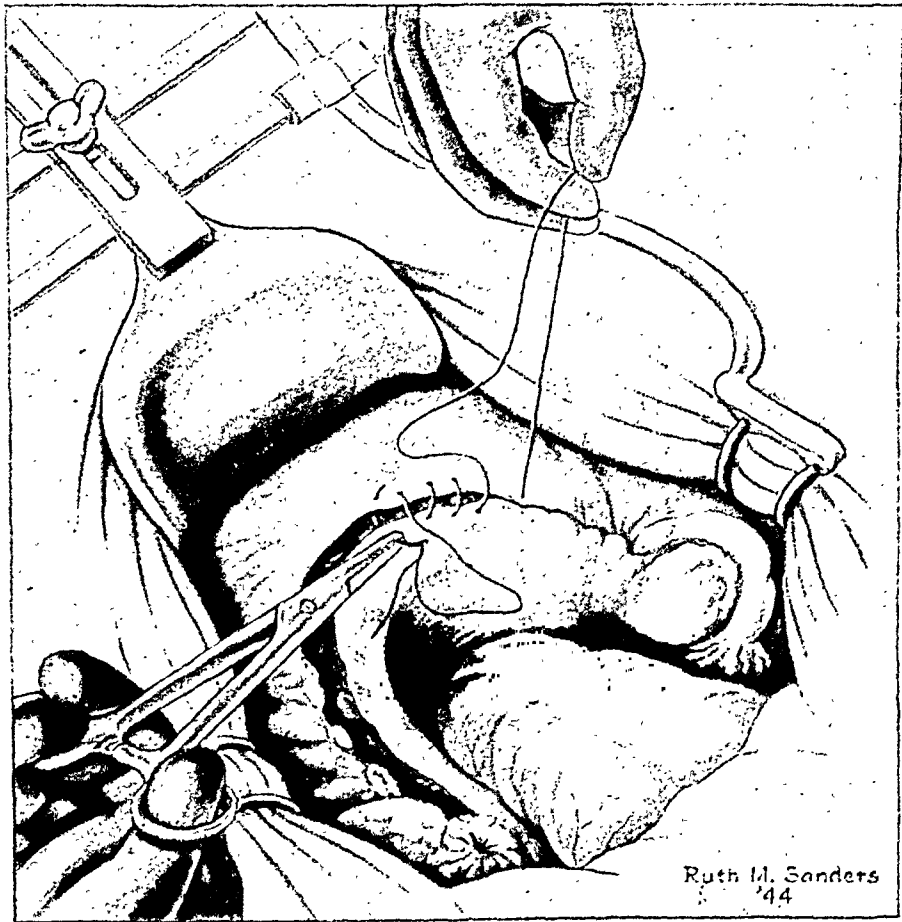


Fig. 6.—Technique of abdominal hysterectomy—peritonization with continuous chromic 00, care being taken to extraperitonize the ovarian and round ligaments and the tubal stumps.

Although the chief complicating factors were adhesions and bleeding, principal concern was associated with large bowel, ureteral, and bladder injuries which occurred twelve, ten, and twelve times, respectively. Our comparative experience suggests that bowel and bladder injury occurs with similar frequency in any type of abdominal hysterectomy. For

example, there were eight bladder injuries in subtotal and twelve in total hysterectomies. Furthermore, the annual incidence of bladder injury was relatively constant. There were six in the first half and six in the second half of the total hysterectomy series. On the other hand, ureteral injury, while not peculiar to, is more frequently associated with total hysterectomy. Such injury may be avoided with accurate anatomic knowledge and careful dissection. Adequate downward displacement of the bladder tends to increase the distance between cervix and ureters. Group experience developing in any clinic with a closely associated staff tends to minimize the frequency of ureteral injury. This point is illustrated by the fact that seven of the ureteral injuries occurred in the first half and three in the second half of the series, incidences of 0.7 and 0.3 per cent, respectively. Some operators at first employed indwelling ureteral catheters in preoperative preparation but tended to discard this technique as they gained experience. The cut ureter was generally reimplanted in the bladder and contributed to death in only one instance. Secondary operation to reimplant the ureter was necessary only once. In general, bladder or ureteral injuries in gynecologic surgery are amenable to correction and heal well if recognized and repaired immediately. The unforgivable sin is failure to recognize the injury before closure of the abdomen. A detailed report of all types of injury during the course of gynecologic operations is in preparation.

Postoperative Course

Morbidity.—A temperature of 100.4° F. was selected as representing the division between normal and febrile postoperative courses. On this basis, 11 per cent (281) of the patients were afebrile and 16 per cent (306) had fever for only one day. Fever persisted no more than three days in 55 per cent, no more than four days in 66 per cent, and no more than five days in 73 per cent. The greatest number suffered the highest fever on the second postoperative day. The highest temperature, irrespective of the day of occurrence, averaged 101.3° F. The average duration of the postoperative hospital stay was 12.7 days, although the limits ranged from seven to more than twenty days.

TABLE V. NATURE OF POSTOPERATIVE COMPLICATIONS

	NUMBER OF PATIENTS
Abdominal wound infection	73
Urinary tract infection	39
Shock necessitating treatment	51
Operative bed infection	44
Thrombophlebitis	27
Peritonitis	23
Superficial separation, abdominal wound	23
Hemorrhage, early	17
Dehiscence	11
Pneumonia	11
Miscellaneous*	76

*Includes septicemia, pulmonary embolus, atelectasis, cardiac failure, late hemorrhage, foreign body, and urinary and bowel fistula.

TABLE VI. NATURE OF SECONDARY OPERATION NECESSITATED BY THE HYSTERECTOMY

	NUMBER OF PATIENTS
Wound closure (16 superficial, 11 dehiscence)	27
Drainage of abscess	9
Control of hemorrhage	5
Relief of bowel obstruction	3
Removal of foreign body	1
Repair of vesicovaginal fistula	1
Implantation of ureter into bladder	1
Miscellaneous	6

In three instances two procedures were done on the same patient.

Nature of Postoperative Complications.—The principal postoperative complications are shown in Table V. Secondary operation was necessitated by the hysterectomy in fifty patients (2.5 per cent) and the required procedures are retailed in Table VI.

Fatalities.—Thirty-eight of the 1,925 patients died, a mortality rate of 1.97 per cent. The trend of the mortality rate is downward as shown in Fig. 7. During 1942, the rate was 0.51 per cent and during 1943 there was no death. In other words, there was only 1 death among the last 335 total hysterectomies. To illustrate the decreased mortality rate in another way, the series was arranged chronologically and divided equally. There were twenty-nine deaths in the first half and nine in the second half of the series, rates of 3.01 and 0.94 per cent, respectively.

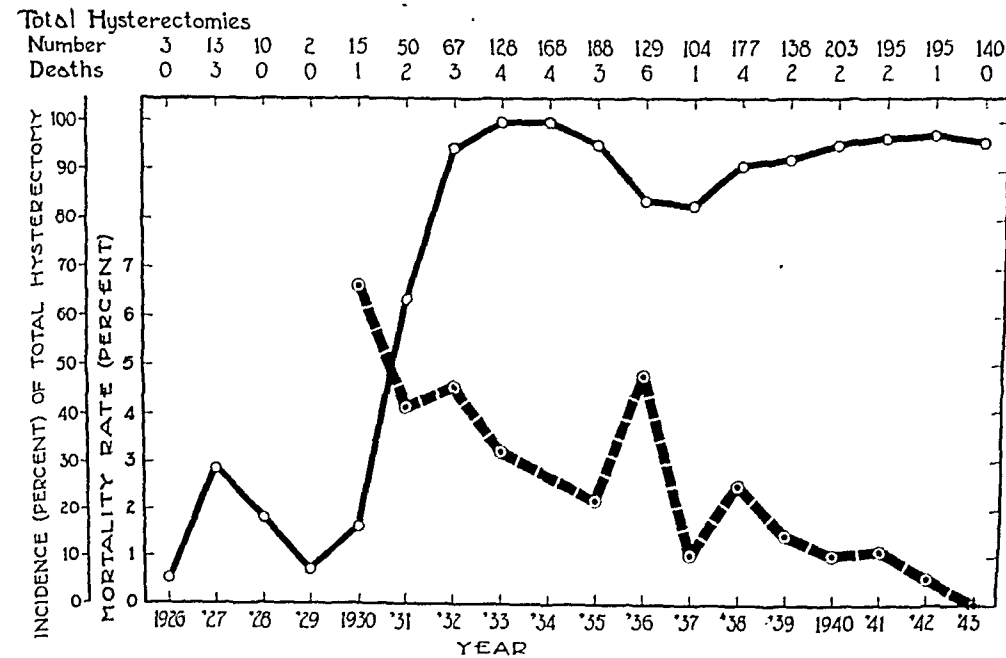


Fig. 7.—Annual incidence and mortality rates of total abdominal hysterectomy. Because of insufficient numbers, the mortality rates for the years 1926 to 1929 were not calculated. The gross mortality rate was 1.97 per cent, but twenty-nine deaths occurred during the first 877 (1926 to 1937, inclusive) hysterectomies and only nine in the last 1,048, rates of 3.08 and 1.05 per cent, respectively. Note that during 1942 and 1943 there was only one death from 335 hysterectomies, a rate of 0.3 per cent.

Postmortem examination was conducted on twenty-seven of the thirty-eight women.

The causes of death are grouped in Table VII. A more detailed study reveals that peritonitis was present in sixteen, pneumonia in six, and septicemia in four patients. Embolism accounted for six of the deaths, a fatality incidence of 0.3 per cent, or 1 in 321. Four of the fatalities occurred following fifty secondary operations, a mortality rate of 8.0 per cent.

TABLE VII. CAUSE OF DEATH

	PATIENTS	
	NUMBER	PER CENT
Infection	22	57.9
Embolus	6	15.8
Exsanguination and shock	3	7.9
Cardiac failure	2	5.3
Other	5	13.1

Comparison of Subtotal and Total Hysterectomy

Detailed comparison between the 393 subtotal and the 1,925 total hysterectomies reveals few essential differences. The subtotal mortality rate was 4.1 per cent, but since almost three-fourths of these operations were performed before 1932, the comparison is not valid.

Morbidity, postoperative complications, and causes of death were very similar in the two series.

The only significant difference lay in injuries to the urinary tract. The bladder was inadvertently opened eight times, 2.0 per cent, in the subtotal hysterectomies as against twelve times, 0.6 per cent, in total removal of the uterus. Bladder injury, therefore, is no more frequent in total hysterectomy and may be less because of the necessity for more adequate dissection.

Ureteral injury did not occur with subtotal but was incurred ten times with total hysterectomy, an incidence of 1 in 193 patients. Obviously a similar incidence with subtotal hysterectomy should have resulted in two such injuries.

Discussion

It is no part of the purpose of this paper to advocate the general adoption of elective total hysterectomy. Largely by circumstance, the Department of Obstetrics and Gynecology of the University of Iowa gave the elective performance of total hysterectomy a trial. The results were satisfying, and we believe we have demonstrated that total hysterectomy, performed mostly by young men in training, is a safe and reasonable operation. It was essential in the 12 per cent of the operations that were performed for malignant disease. If it be granted that removal of the cervix is desirable in the presence of pelvic inflammatory disease, then total hysterectomy was desirable in an additional 329 patients. In other words, removal of the cervix was essential or desirable in 563 patients, or 2 in 7. Any university department of obstetrics and gynecology actively engaged in training young men must, therefore, face the necessity of teaching the techniques of total hysterectomy. Since any technique improves with performance, and since this technique is a necessity for the gynecologic surgeon, it would seem that adequate training is desirable.

If elective total hysterectomy introduced a great hazard to the life, health, or happiness of the patient, such a position would be untenable. Since this is not the case, and since the results of this series can be duplicated in any acceptable institution, it would seem that our obstetric and gynecologic residents should be given the opportunity to acquire the technique of total hysterectomy.

Summary and Conclusions

1. Total abdominal hysterectomy was performed on 1,925 women, most of whom were white and indigent.

2. The majority of the patients (59.3 per cent) remained in the hospital from two to five days before operation. Only 12.4 per cent were operated on within twenty-four hours of admission.

3. The majority of the operations (63.4 per cent) were done by assistant residents or residents.

4. The principal indications for hysterectomy included fibromyoma, functional bleeding, pelvic inflammatory disease, benign and malignant ovarian and malignant uterine tumors.

5. Ureters were injured in ten women, with nine repairs, at the time of initial operation. Subsequent operation for reimplantation was necessary in one patient.

6. Morbidity rates were similar to those of any hysterectomy series, irrespective of the type of operation.

with infarction of varying degrees very frequently occur without presenting the complete classical picture. The fatal pulmonary embolism is usually preceded by "warnings" if we could but interpret the symptoms. In suspected cases, an x-ray of the chest taken within three or four hours is of distinct diagnostic value. If such is not practicable, at least dicoumarin therapy in prophylactic doses should be immediately instituted. Since the physiologic response of dicoumarin is not obtained within forty-eight hours, heparin, which has an almost instantaneous effect, should be given over this induction period of forty-eight hours at the rate of 5 mg. in continuous intravenous saline infusion.

We have not had the same unfortunate experience as Dr. Mengert in damage to pelvic viscera: namely, the bowel, bladder, and ureters. Damage to the bladder should be a very rare accident unless its walls are deeply infiltrated by the existing morbid process.

At this point I should like to make a plea for the better training of our residents and junior attending staff in anatomy, as without a thorough practical knowledge of this subject one cannot hope to avert disaster. Accidents to pelvic viscera are, by and large, in exact proportion to the knowledge of practical and applied anatomy, which can be obtained only by a special training in the dissecting room.

DR. F. S. WETHERELL, SYRACUSE, N. Y.—I would like to discuss two phases of this paper: namely, deaths from infection and embolic deaths. I would like to ask Dr. Mengert how he prepares the vagina preoperatively? In some large clinics I have watched total abdominal hysterectomies performed with no gauze used in the preoperative preparation of the vagina. With a patient in Trendelenburg position, under spinal anesthesia, it is well to pack the vagina with gauze to prevent possible seepage of rectal contents into the vagina incident to relaxation of the anal sphincter.

Pulmonary embolism or pulmonary infarct, which usually occur within the first seven to ten days, are often not recognized by the gynecologist when the first symptoms begin to manifest themselves. He fails to realize the complete significance of a normal temperature or low-grade fever which suddenly changes and goes up a degree or more. At that time the patient herself will often complain of feeling uneasy and apprehensive. Those two little preliminary symptoms are important. He now fails to feel the calf muscles, to make pressure on the soles of the feet, and to do the Homan test of extending the feet on the legs. There is a time when it is perfectly proper to feel a woman's legs: namely, on the first day postoperatively. Thus the patient becomes accustomed to the amount of pressure made daily thereafter on the calf of the leg and on the sole of the foot; if there is a change toward tenderness, she will tell you.

An embolic death is a terrible thing and it can be avoided by careful routine examination. If tenderness and the other signs are present, there should be an immediate ligation of the femoral vein—not the institution of heparin or dicoumarin therapy. The thrombus as a rule starts in the veins of the soles of the feet and travels upward in the external saphenous which becomes the popliteal and then the femoral vein. The way to stop an embolus from getting into the lung or pulmonary artery is to tie off the vein. Even the common iliac vein can be tied with impunity. For that matter, the inferior vena cava has been tied. I would make a plea now that pelvic surgeons drop about an inch below the pelvis and learn how to do a ligation of the femoral vein because they may not have a general surgeon handy to do it.

DR. W. S. BAINBRIDGE, NEW YORK, N. Y.—I wonder if it would not have been of advantage to have made a thorough examination of the blood previous to operation in these cases? We examine for syphilis and some, like myself, also have the sugar content tested when the operation is not an emergency. As we frequently employ glucose after operation I believe that preoperative examination of the blood as to sugar content would be a move toward making the patient safer for the surgery. I noted also that among the cases reported there were a good many of excessive bleeding. A routine test for coagulation time, followed by proper medication if necessary, might have been of advantage.

In quite a number of the cases cyclopropane was employed. Certain of our large hospitals in New York refuse to permit any of it in the building as explosions and

a number of deaths have occurred from its use. What advantages does the author consider that it has over other anesthetics?

DR. MENGERT (closing).—Our patients were kept in the hospital from two to five or more days preoperatively and only a small number of them were operated upon within twenty-four hours. In general, they had careful and adequate preoperative preparation. Regarding Dr. Bainbridge's question, I think the coagulation time was generally omitted in these patients and it is likely that attention to this point may have prevented some of the bleeding. On the other hand, I think that a good deal of the bleeding might have been due to inexperience and the fact that these young men were learning.

In regard to Dr. Wetherell's question, we carefully prepared the vagina by scrubbing with green soap and water, painting with the antiseptic of choice which has varied through the years and, of course, the patient was catheterized. When the vagina was opened anteriorly a loosely fluffed sponge was immediately inserted to absorb any of the vaginal antiseptic that might be there. We have never made a practice of preparing the vagina in cesarean section. Quite a number of the cesarean hysterectomies were total hysterectomies and those patients get along perfectly well without any vaginal preparation. How important vaginal preparation is I do not know, but it was carried out routinely with the exception noted.

Our principal prophylaxis with regard to embolus has been to insist that the patient be turned from side to side and encouraged to move around freely. In recent years we have been getting patients up very early after operation. In general they have remained in bed nine or ten days, but a few of them have been treated with early activity and early rising from bed.

Cyclopropane alone certainly does not give adequate relaxation for pelvic surgery. At times patients returning from the operating room after that anesthesia have gone into shock, possibly attributable to the anesthetic. We have had no explosions and no suggestion of them although cyclopropane and ethylene have been in use at Iowa for a long time. The principal reason why cyclopropane has been used lately lies in the use of curare. The two seem to work very well together and the patient needs to be put into only a light anesthesia, barely rendered more than unconscious, and the musculature can be relaxed and the relaxation maintained for the duration of the operation.

END RESULTS IN THE TREATMENT OF CERVICITIS*

DAVID FINDLEY, M.D., OMAHA, NEB.

(From the Department of Obstetrics and Gynecology University of Nebraska,
College of Medicine)

IT WAS Carl Ruge of Berlin who, at the turn of the twentieth century, first demonstrated the pathology of cervicitis, and there followed a general understanding of the clinical significance of the lesion. But there remains to be developed a more uniform agreement on the choice of procedures to be applied in the management of the various phases of cervicitis. There is fairly universal acceptance of the therapeutic value of the cautery but there still is much confusion as to the type of cautery best suited for the individual case. With this in mind I have endeavored to determine for my own satisfaction the respective merits of the several methods of cauterization now in vogue, and to this end I have accumulated a series of observations on biopsies, both before and after cauterization, this to determine the method most favorable to complete healing and freedom from ensuing complications.

*Read by invitation at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1944.

All types of cervical infections should be classified under the one heading—cervicitis. Subheadings, such as endocervicitis, erosion, cystic cervicitis, etc., merely designate the degree to which the pathologic process has advanced. Fundamentally the progression of tissue changes in all these conditions is quite similar—infection is followed by congestion with hypersecretion of the cervical glands, granulation tissue is infiltrated with polymorphonuclear leucocytes and bacteria. There is desquamation of the squamous cells covering the portio, and finally replacement by columnar epithelium.

Curtis¹ and Miller² both state that the columnar epithelium grows faster than the squamous type and is more resistant to chemical and bacterial irritants. It follows that irritation subsides and the more hardy and healthy squamous epithelium replaces the columnar cells, leaving scattered nabothian cysts and fibrous tissue.

Culbertson³ asserts that follicular erosions show an attempt at healing in which the ducts are occluded thereby giving rise to cystic formations. The presence of squamous cells on the surface suggests metaplasia, although Baer⁴ is of the opinion that these islets of squamous epithelium remain in the zone of the lesion and aid in rapid epithelization of the portio. Squamous cells in the gland lumen or stroma surrounding the glands suggest direct cellular proliferation and may be confused with carcinoma.

The sequelae of cervicitis are many and varied.⁵ There may simply be local manifestations, namely, leucorrhea, pruritis, frequency of urination, dysmenorrhea, and dyspareunia with possible resulting sterility. It may act as a focus of infection. Last, and of utmost importance, cervicitis is definitely a precancerous lesion. Phaneuf⁵ in 100 consecutive biopsies of well-advanced cervicitis found primary carcinoma in 10 per cent. J. Davis⁶ asserts that proper treatment would cause a 90 per cent reduction of cervical carcinoma. Although most authors cite a lower incidence of malignant change, it is generally accepted that carcinoma is a frequent sequel of cervicitis and that early irradiation of the lesion is the most effective prophylactic measure we possess. In this, I heartily concur.

A multitude of methods have been advanced for the treatment of cervicitis. Many have been discarded and some variations in technique have been introduced. At the present time the therapeutic procedures employed are topical chemical agents, autogenous vaccines, heat, cold, surgery, and electrosurgery. Novak⁷ states that caustics have some value in mild superficial infections but may cause stricture, while C. J. Miller⁸ and Black,⁹ among many, opine that topical chemical applications are of no value. However, as shown in Table II, I believe that beneficial results can be obtained by such chemicals where there is incomplete healing following other more drastic procedures. As for autogenous vaccines, they are, in my opinion, of questionable value in the treatment of cervicitis.

Heat therapy, in the form of diathermy, has among its advocates Corbus and O'Connor¹⁰ in the treatment of gonorrheal endocervicitis. The Elliot treatment has been advocated by Holden and Gurnee.¹¹ However, this procedure has few enthusiastic supporters.

Carbon dioxide snow has given some beneficial results according to Curtis¹ but its place is extremely limited.

Surgery in the form of trachelorrhaphy, tracheloplasty, and amputation has for years had many supporters. All, I think, will agree with Phaneuf,¹² Black,⁹ and Miller¹³ that trachelorrhaphy is at times indicated in women during the childbearing age and amputation or the Sturmdorf operation in the postmenopausal stage. Matthews¹⁴ is of the opinion that the Sturmdorf tracheloplasty does not interfere with labor

to a greater degree than trachelorrhaphy, and Mason¹⁵ believes, as do I, that the Sturmdorf operation is the best of all surgical procedures.

During recent years electrosurgery has almost completely replaced all other types of treatment for cervicitis. These procedures are grouped under three heads: actual or nasal tip cauterization, electrocoagulation, and conization. Each of these has a definite place in our therapeutic armamentarium and each has its advocates.

It is said that Hunner¹⁶ was the first to adopt the actual cautery with the accepted radial stroke technique. His best results were obtained in hypertrophy and erosion following childbirth. In his experience hemorrhage was frequently encountered. Moench and Schulman¹⁷ claim that the actual cautery is superior to all other methods in the treatment of nabothian cysts and prefers electrocoagulation in all other types of cervicitis. Goodall and Power¹⁸ obtained best results with electrocoagulation in superficial infections but point out the dangers of stenosis in deep carbonization. Baer⁴ reports fifteen years of office cauterization with only two late hemorrhages and one stricture. Matthews¹⁹ advocates the use of the actual cautery for recent and superficial infections but not for the more extensive lesions. Mason,¹⁵ in the use of the actual cautery, warns of fibrosis with contraction and the uncertain extent of tissue destruction. Masson and Powers²⁰ point out still another complication, namely, pelvic abscess. Cashman²¹ advises the passing of a sound at intervals for at least ten weeks following cauterization to forestall stenosis of the cervical canal. I personally feel that the nasal tip cautery is an excellent agent for the treatment of early postpartum erosions but not for the extensive long-standing cases because of the danger of hemorrhage and stenosis.

Electrocoagulation has gained many advocates in the past few years. Frost²² finds that healing takes place with a minimum of scar tissue except when used with high voltage. He asserts that healing occurs in about four weeks but warns that the method should not be employed in the presence of pelvic inflammation. Black⁹ is of the opinion that electrocoagulation is more apt to be followed by infection than is either cauterization or conization, listing hemorrhage, stenosis, atresia, cellulitis, pelvic abscess and peritonitis as occasional complications. He wisely points out that penetration of the uterine cavity increases the danger of infection. Maryan²³ and Moench and Schulman¹⁷ list the advantages of electrocoagulation over other methods. These include: (1) a controllable, uniform penetration with minimum carbonization; (2) more rapid destruction of diseased areas; (3) no accidental injury because the current is easily controllable; (4) less scar tissue formation. The above is an impressive array of advocates of electrocoagulation, but it is to be observed that though electrocoagulation is in universal practice there is a wide discrepancy in many of the details both in technique and in indications.

Hyams²⁴ was one of the first to adopt conization in the treatment of cervicitis. He claims the beneficial results were due to the removal of the diseased glands, that the danger of hemorrhage was almost nil, and that resultant scar tissue was minimal. This, in my experience, is refuted by Table V and also by numerous cases not included in my report. Boland²⁵ reports that conization produces a thin layer of coagulation and desiccation which does not interfere with primary healing but does tend to prevent bleeding and infection by sealing over the blood and lymph channels. In his cases healing occurred in four to eight weeks. Stadium²⁶ would perform conization in hypertrophy and elongation of the cervix and says that though there were frequent hemorrhages subsequent labors were not interfered with. Royston²⁷ reports that hemorrhage was present in 11½ per cent of 275 cases and that scar tissue formation was greater than that following electrocoagulation. N. F. Miller²⁸ observed stenosis in from 6 to 10 per cent of cases following conization. Novak⁷ states that, in general, conization is less favor-

able than other methods in the treatment of cervicitis. Here again we find the authorities quoted above fall short of agreement on many details. For my own part, I have abandoned conization for fear of hemorrhage, which in my hands has occurred to an alarming degree as late as the third week following operation.

Personal Observations

My series includes 240 cases of chronic cervicitis, with or without erosion, cysts, eversion, or hypertrophy. No immediate postpartum lesions are included. I have endeavored to determine the degree of healing in the various groups. These groups include the cases treated by the accepted methods of cauterization, to wit, nasal tip, coagulation, and conization. The number of treatments are recorded, the degree of sloughing is noted, as are the complications following the application of the cautery.

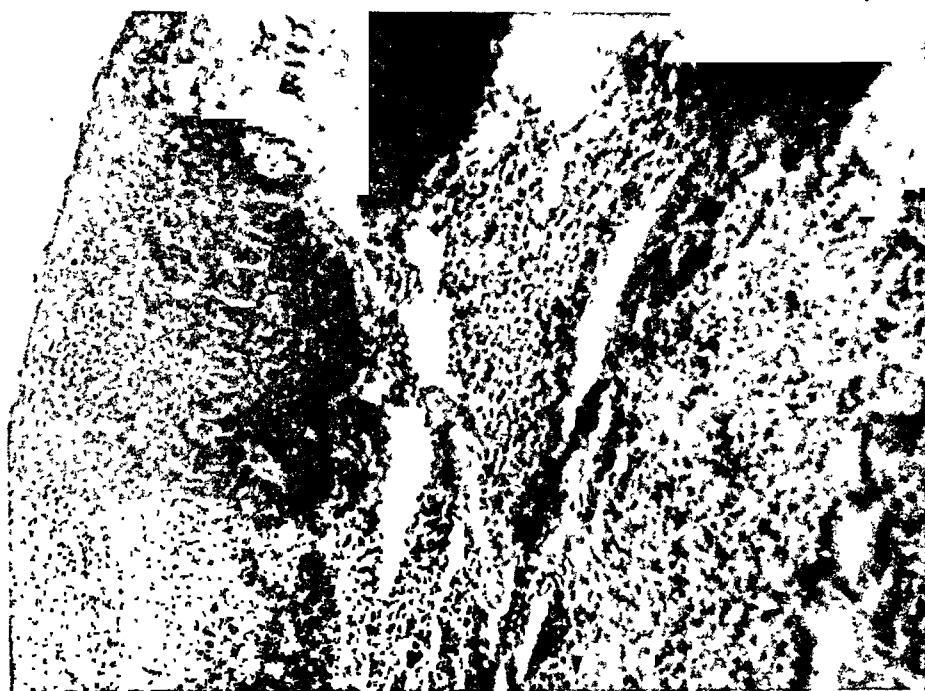


Fig. 1.—Mrs. G. M. Biopsy Sept. 4, 1941. Chronic cervicitis with erosions showing dense submucous leucocytic infiltration and desquamation of squamous epithelium. Treated by nasal tip cautery.

Table I includes the total number of cases with varying degrees of erosion and the type of treatment employed.

TABLE I. TOTAL CASES—240

DEGREE OF EROSION	NASAL TIP	COAGULATION	CONIZATION
None	22	24	20
First degree	28	24	4
Second degree	32	30	21
Third degree	15	8	12
Total	97	86	57

All nasal tip cauterizations were done in the office and were superficially done because of lack of anesthesia. Those treated by electrocoagulation and conization were hospitalized and a more thorough treatment was carried out under general anesthesia.

Table II reveals the number of patients requiring one or more treatments before satisfactory results were obtained. As noted, several cases were treated with topical applications as well as by electrosurgery.

TABLE II. NUMBER OF PATIENTS

NUMBER OF TREATMENTS	NASAL TIP	COAGULATION	CONIZATION
1	56	52	57
2	22	15	0
3	4	10	0
4	6	1	0
AgNO ₃ -25%	9	8	0
Total	97	86	57

This report differs from others published advocating electrocoagulation. Fine²⁹ states that in his series 39 per cent required but one treatment, 61 per cent, two or more. Baumrucker and Baumrucker³⁰ claim that 82 per cent were healed after one coagulation. In my series 52 required but a single treatment; 34 required two or more treatments.

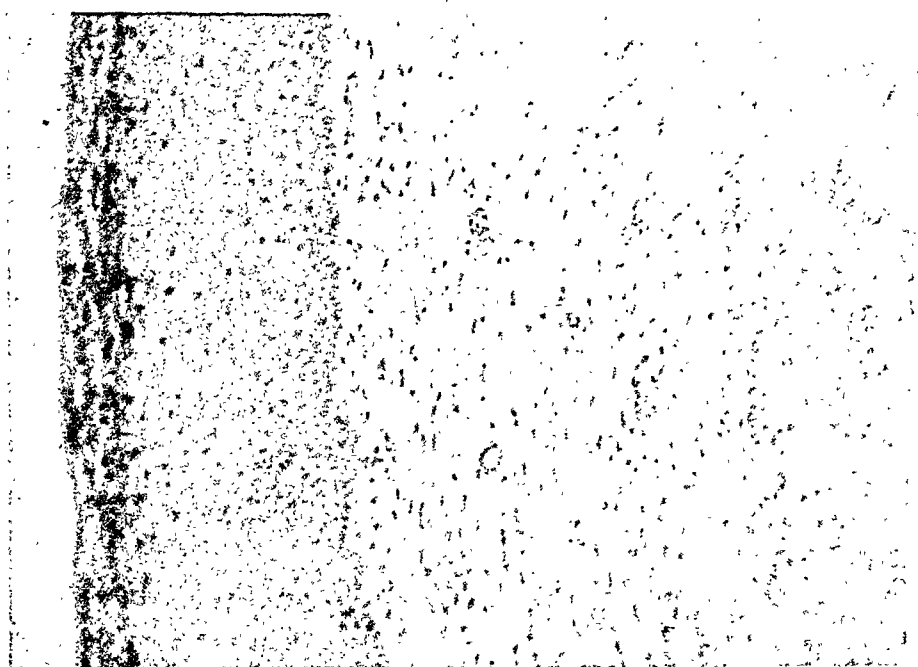


Fig. 2.—Mrs. G. M. Biopsy of anterior lip Nov. 6, 1941, showing complete healing with minimal fibrosis and obliteration of blood vessels.

An attempt was made by close follow-up to determine the reactions of cervical tissue to these various methods of treatment. As far as possible cases were observed at weekly intervals. However, as many of the patients seen came from scattered sections of the state, subsequent checkups were made through the cooperation of the local physicians. Unfortunately, because of war priorities, equipment was not available to photograph the cervix during these stages in order to show the gross changes taking place during the early weeks following treatment. For a characteristic photographic record the reader is referred to the article previously mentioned.²⁹

It is noted in Table III that there is a very little difference in elapsed time among the three classifications as to when the slough is at its height, when it is completely separated and granulation and epithelization begin, and when healing is clinically complete.

These figures vary markedly from those of Jacoby²¹ who found clinical cures from the cautery in four months, coagulation in seven months, and conization in 7.3 months. Baumrucker and Baumrucker²⁹ claim

TABLE III

HEALING	NASAL TIP	COAGULATION	CONIZATION
Slough at height	7 days	9 days	9 days
Slough separated	17 days	19 days	15 days
Healing complete	7½ weeks	7½ weeks	7+ weeks

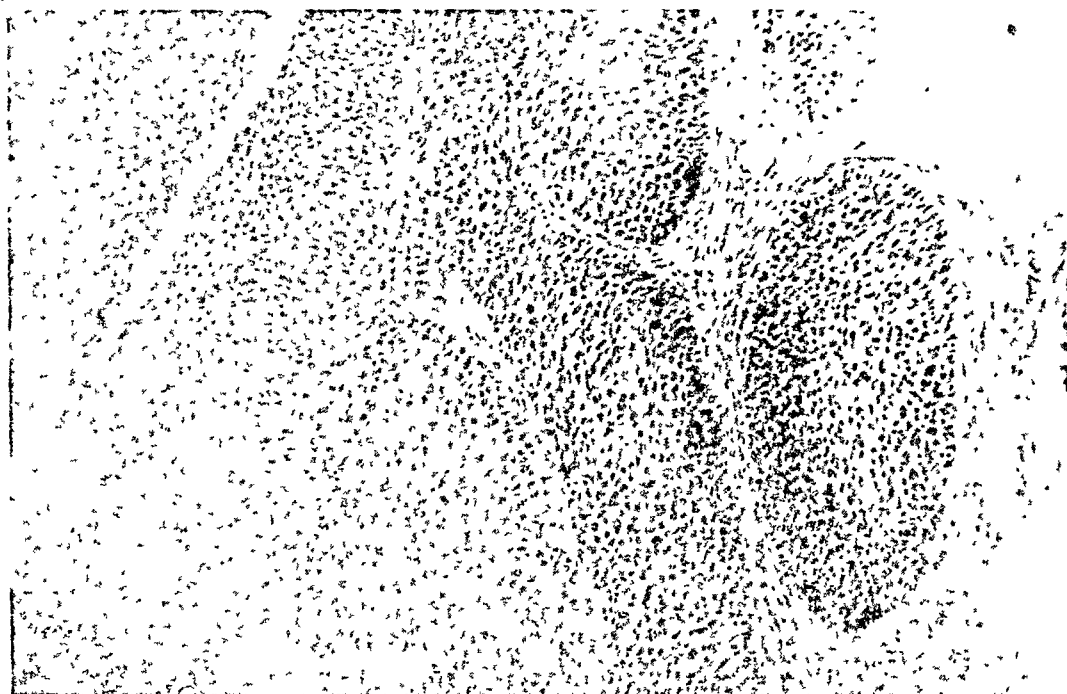


Fig. 3.—Mrs. G. M. Biopsy of posterior lip Nov. 6, 1941, showing a Grade II squamous cell carcinoma overlooked in previous biopsy.

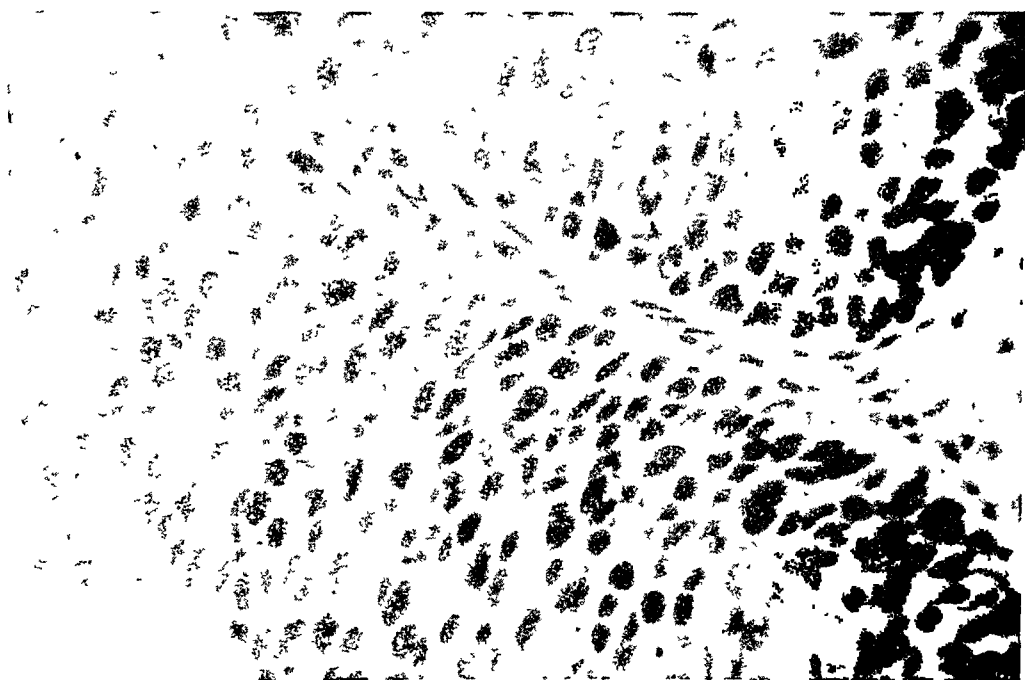


Fig. 4.—Mrs. G. M. High magnification of Fig. 3.

healing occurred in ten weeks or less in 75 per cent of cases following coagulation. Barrett³² reports healing in from four to six weeks and Kimble³³ in six to eight weeks.

It is apparent that the large percentage of subsequent endocervicitis and erosion following treatment, as seen in Table IV, resulted because the electrosurgical procedure was not carried high enough in the cervical

canal to reach and destroy all of the infected cervical glands. There was little excuse for this in the series done by electrocoagulation and conization because these patients were under surgical anesthesia. All cases treated by the nasal tip method were handled in the office without anesthesia so that a thorough and complete procedure was seldom carried out.

In Table IV we observe the percentage of cures and less favorable end results. Under the term "endocervicitis" are included all cases seen with a subsequent excessive mucoid or mucopurulent discharge.

TABLE IV. END RESULTS

RESULTS	NASAL TIP (%)	COAGULATION (%)	CONIZATION (%)
Healing	50	78	72
Erosion	24	9	3
Endocervicitis	24	12	25
Failure	2	1	0

TABLE V. COMPLICATIONS

COMPLICATIONS	NASAL TIP	COAGULATION	CONIZATION	TOTALS
Carcinoma	1	0	1	2
Hemorrhage	0	2	4	6
Stenosis	0	1	4	5
Pyometra	0	1	1	2
Infection	0	0	0	0

Most authors agree that certain complications are bound to result no matter what type of treatment is employed. The complications most often observed are hemorrhage, stenosis, pyometra, and pelvic inflammatory reaction. A few essayists stress the importance of suspecting carcinoma in cases which do not respond to local treatment. Table V reveals the complications noted in my limited series. Both of the cases of carcinoma were recognized only by microscopic examination of routine biopsied tissue. Neither was suspicious macroscopically. One of these patients was biopsied on first observation and reported as purely a benign inflammatory process. Upon repeated treatments, however, the lesion failed to heal, and subsequent biopsy revealed a low-grade squamous cell carcinoma.

Hemorrhage occurred in six of the 240 cases. In two of these, both following conization, the amount of bleeding was alarming, and one required transfusion to replace the blood loss. I have seen several other cases not included in this report that had had repeated profuse hemorrhages following conization. One required thirteen transfusions and three attempts at suturing the cervical branch of the uterine artery before recovery occurred. Karnaky²⁴ reports 1 per cent hemorrhage following electrocoagulation, 3 per cent after cauterization and conization alike.

Stenosis of the cervical canal occurred most frequently following conization. The principal reason for this is that many of these cases were not under my control, and periodic dilation of the cervix was not done by the patient's local physician.

Presented in this series were several obstinate cases which, after repeated cauterization, revealed no beneficial results. On questioning these

patients it was found that they were using internal menstrual tampons. Repeated cauterization and a change in the type of protection resulted in prompt healing. The results are noted in Table VI.

Karnaky³⁴ reports end results in the treatment of cervicitis. He claims conization is superior to other methods, that it gives but a 1 plus or 2 plus fibrous tissue reaction and obliteration of blood vessels. Coagulation was followed by a 2 plus fibrosis and cautery by a 4 plus reaction. In my study of cases reported, the above figures were varied. A low fibrous tissue reaction following nasal tip cautery was found because all cases were treated lightly. There was little difference between coagulation and conization in the end histological pictures. These reactions were slightly more pronounced than after nasal tip cauterization.

Conclusions

1. Two hundred and forty cases of chronic cervicitis were treated by the three generally accepted methods of electrosurgery, namely, nasal tip cauterization, electrocoagulation, and conization.

2. Histological studies were made before treatment and after healing was clinically complete.

3. Comparisons were made as to the rate and type of healing following each therapeutic measure and also as to resultant complications.

4. The average rates of healing were found to be the same with all three methods.

5. The percentage of satisfactory results was greatest after electrocoagulation, second after conization, and least following cauterization.

6. There was very little difference between coagulation and conization in the end histological picture. Fibrous tissue reaction was very low in both procedures although slightly greater following cauterization.

7. Complications most commonly encountered were hemorrhage, stenosis, and pyometra, and were most frequently seen following conization.

8. Hemorrhage usually occurs from the tenth to the fifteenth day at the time of separation of the slough.

9. Stenosis with resultant pyometra may be largely prevented by repeated dilation of the cervical canal.

10. Carcinoma was discovered in two unsuspected cases out of 240 examined.

11. Internal menstrual tampons were found to interfere with proper healing. Their use is to be condemned.

I wish to express my appreciation to Mrs. Glenn Streby for her cooperation in the preparation of the microscopic slides and to Dr. Charles Baker for his help in preparation of the photomicrographs.

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References

1. Curtis, A. H.: Textbook of Gynecology, ed. 4, Philadelphia, 1942, W. B. Saunders Co., Chap. 40.
2. Miller, N. F.: J. Michigan M. Soc. 35: 75, 1936.
3. Culbertson, C.: J. A. M. A. 87: 1808, 1926.
4. Baer, J. L.: J. A. M. A. 111: 2357, 1938.
5. Phaneuf, L. E.: New England J. Med. 220: 859, 1939.
6. Davis, J.: Tr. Am. Ass. Obst. & Gynec. 44: 1931.
7. Novak, E.: Gynecology and Female Endocrinology, Boston, 1931, Little, Brown & Co.
8. Miller, C. J.: J. A. M. A. 87: 1695, 1926.

9. Black, W. T.: J. A. M. A. 112: 191, 1939.
10. Corbus, B. C., and O'Connor, V. J.: J. A. M. A. 87: 1816, 1926.
11. Holden, F. C., and Gurnee, W. S.: AM. J. OBST. & GYNEC. 22: 87, 1931.
12. Phaneuf, L. E.: Am. J. Surg. 36: 226, 1937.
13. Miller, C. J.: Surg., Gynec. & Obst. 46: 337, 1928.
14. Matthews, H. B.: J. A. M. A. 87: 1802, 1926.
15. Mason, L. W.: Colorado Med. 33: 177, 1936.
16. Hunner, G. L.: J. A. M. A. 46: 191, 1906.
17. Moench, G. L., and Schulman, A.: M. J. & Rec. 131: 131, 1930.
18. Goodall, J. R., and Power, R. M. H.: AM. J. OBST. & GYNEC. 33: 1050, 1937.
19. Matthews, H. B.: Am. J. Surg. 36: 233, 1937.
20. Masson, J. C., and Powers, E.: AM. J. OBST. & GYNEC. 16: 348, 1928.
21. Cashman, B. Z.: AM. J. OBST. & GYNEC. 41: 216, 1941.
22. Frost, I. F.: Am. J. Surg. 34: 221, 1936.
23. Maryan, H. O.: M. Clin. North America 27: 83, 1943.
24. Hyams, M. N.: Arch. Phys. Therapy 11: 171, 1930.
25. Boland, B. F.: New England J. Med. 205: 434, 1931.
26. Stadium: Arch. Phys. Therapy 19: 398, 1939.
27. Royston, G. D.: South. M. J. 26: 44, 1933.
28. Miller, N. F.: California & West. Med. 47: 81, 1937.
29. Fine, S. G.: J. M. Soc., New Jersey 33: 507, 1936.
30. Zelezny-Baumrucker, O., and Baumrucker, G. O.: Surg., Gynec. & Obst. 67: 17, 1938.
31. Jacoby, A.: AM. J. OBST. & GYNEC. 36: 656, 1938.
32. Barrett, R. L.: J. A. M. A. 103: 1516, 1934.
33. Kimble, H. E.: Arch. Phys. Therapy 14: 550, 1933.
34. Karnaky, K. J.: Radiol. Rev. & Mississippi Valley M. J. 60: 127, 1938.

Discussion

DR. WALTER T. DANNREUTHER, New York, N. Y.—No single therapeutic method is applicable to all cases of infection and damage resulting from birth trauma indiscriminately. Where there has been a recent transverse laceration with simple ectropion, without infection, stripping of the eroded areas with a fine wire cautery tip, repeated two or three times at three-week intervals, will result in retraction and contraction and satisfactory healing. For cases of deep-lying infections in the compound racemose glands of the endocervix, conization will completely remove the diseased tissue with no damage to the rest of the portio, provided a very high tension current which is free from any desiccating effect and the original Hyams electrode are used, and the technique described by Hyams is followed exactly. Under such circumstances, hemorrhage, stenosis, or pyometra should never occur. For the multiparous woman with an extensively scarred, cystic, and infected cervix, extirpation is the safest method of treatment, and personally I prefer hysterectomy, either vaginal or abdominal, to amputation. The greatest disadvantage of electrocoagulation is the operator's inability to control the depth of heat penetration and consequent destruction of tissue, and in my experience it has been the most common cause of cervical stenosis, dystocia at the time of labor, and secondary hemorrhage. The sole virtue of silver nitrate applications lies in their ability to stimulate the proliferation of squamous epithelium.

I believe that Dickinson and not Hunner should be credited with originating cauterization for the treatment of endocervicitis.

Perhaps the differences in the viewpoint of Dr. Findley and myself can be explained by technical variations in his hands and mine.

DR. MELVIN A. ROBLEE, St. Louis, Mo.—For the past fourteen years in the Washington University School of Medicine Outpatient Department in St. Louis we have had all cases of cervicitis referred for therapy to the cervicitis clinic. The assistant resident, under close personal supervision, has had this as his clinic for a six-month period. Each year a few cases of chronic cystic cervicitis are cauterized with nasal tip cautery by the intern who will become the assistant resident. He again sees these patients six months to one year later in order to demonstrate the temporary nature of noted improvement.

Our assistant residents are instructed to use a conization electrode only one time within the cervical canal, never to recut except to undermine the cervical lips of the external portion of the cervix with another electrode which locates the cutting element in the proximal portion only. The distal part in contact with the internal

os contains no cutting element. An ordinary biopsy loop could be used to undercut the external portion of the cervix which contains nabothian cysts.

For the past two years we have directed attention to the local application of sulfonamides to the coned cervix at the time of operation and as postoperative care. Healing time is much faster. Complicating secondary hemorrhage and stenosis have been reduced. Unless great care is exercised not to damage the internal os of the cervix, conization will be limited to women past the childbearing age. On the other hand, if deep cutting is limited only to the nabothian cystic areas of the external portion of the cervix, and if sulfonamides are used locally postoperatively, good clinical results have been our experience.

DR. FINDLEY (closing).—I agree with Dr. Dannreuther that great care should be taken in the application of any and all procedures involved in the cauterization of tissues. To this end we have on numerous occasions applied the cautery to raw meat to demonstrate the extent of its penetration. We are mindful of the fact that excessive carbonization may lead to stenosis and hemorrhage.

I have followed Dr. Roblee's technique of applying sulfonamides in buffered acid jelly to the cauterized cervix on a number of patients with gratifying results, although there were not a sufficient number of cases to be included in this paper.

SEX PRECOCITY, VIRILISM, ADRENAL CORTICAL TUMOR*

J. P. PRATT, M.D., AND ROBERT L. SCHAEFER, M.D., DETROIT, MICH.

(From the Henry Ford Hospital)

SEX precocity assumes practical importance as a physical and psychologic problem. By comparison of the three cases presented here, two of the patients are quite obviously precocious while the third is only border line. Although certain standards are accepted as normal, one must permit considerable variation in both time and degree of development. The life of an individual consists of a series of transitions from one phase to another. The neutral segmenting ovum soon develops to a stage at which the gonads indicate the male or female future. At birth, all of the sex characters are present, though some of them are rudimentary. Through childhood, puberty, and adolescence, the development continues to maturity. Disturbance of development during childhood may result in sex precocity.

Sex differentiation is complex. Though one believes that genes determine whether the gonad will be male or female and that the gonads primarily control the determination of the sex characters, the secondary factors that control the function of the gonads are not so readily correlated.

Classification of sex precocity is difficult because no two cases reported are exactly alike. The alteration in development may be due to (1) endocrine hyperfunctional tumors (adrenal, ovary, testis), (2) endocrine hyperfunction with or without cellular hyperplasia, (3) tumors in the region of the third ventricle, and (4) pineal tumor.

Sex precocity is not rare, nor can it be considered uncommon. In a former study by one of us (R. L. S.) a survey of 2,311 delinquents

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in the preadolescent and adolescent age groups revealed that sex precocity occurred in thirteen, or 6.8 per cent, of the patients. It is desirable that many cases be reported for comparison. Three cases are presented here.

CASE 1.—T. P. was referred by Dr. G. A. Domzalski. She was 2 years, 9 months old when seen April 3, 1937. The diagnosis was virilism and adrenal cortical tumor. One month before the first visit to the doctor, the mother had noticed an unnatural swelling of the genitals. It was assumed that the child had been injured by a fall a few days previously. The development of the child had been normal except for recent rapid growth, change in the genitals, and development of pubic hair. Family history and past history were essentially negative. The child had measles and chicken pox at 8 months without complications.

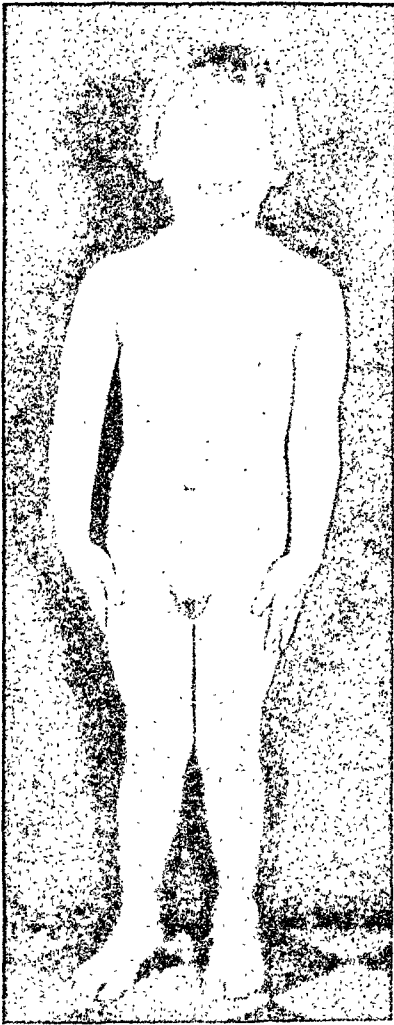


Fig. 1.

Fig. 1.—Case 1. Taken at the age of 2 years, 9 months. Shows masculine trend and precocious development.



Fig. 2.

Fig. 2.—Case 1. Taken at the age of 2 years, 9 months. Shows the large labia minora, clitoris, and coarse pubic hair.

Physical examination: The child appeared large for her age. Her actions were more mature than expected. The muscular development was masculine (Fig. 1). The nose was large and bulbous. The deep voice was startling. The color of the hair was light, the texture fine, and the distribution scant. The pubic hair was coarse, stiff, and black. The enlarged clitoris protruded between the relatively large labia minora (Fig. 2). A small bluish tip on the end of the clitoris suggested a glans. The labia majora were enlarged. The vagina and vestibule were congested and secreted a mucoid substance.

	ACTUAL	NORMAL VARIATIONS
Weight	36.0 pounds	21.7-30.7 pounds
Height	39.0 inches	33.9-36.3 inches
Span	40.0 inches	32.4-34.8 inches
Upper measurement	22.0 inches	19.6-21.0 inches
Lower measurement	17.0 inches	14.0-15.4 inches

Laboratory procedures: The following laboratory tests were done and all were found to be entirely within normal limits: urinalysis, blood count, blood sugar, blood nonprotein nitrogen, blood calcium, blood phosphorus, blood cholesterol, Kahn, basal metabolism. Roentgenogram of the skull revealed a normal sella turcica. Osseous development was studied by roentgenogram of the following joint regions: shoulder, elbow, wrist, hip, and ankle. An advance in osseous development of three years was evidenced. A flat plate of the abdomen was negative. Bio-assay of the urine on two separate occasions, reported by Dr. Oliver Kamm, was negative for estrogens and androgens.

During six months of observation the patient increased six inches in height and gained twelve pounds due to continued muscular development. The voice was deeper, the pubic hair increased slightly, and the external genitals were more conspicuous. A few coarse hairs appeared around the nipples. Hair began to develop in the axilla.



Fig. 3.—Case 1. Adrenal cortical tumor which measured 5.5 by 1.5 by 3.3 cm.

Operation, Jan. 15, 1938: The abdomen was opened by right rectus incision. Exploration of the pelvis showed the uterus to be about the size of the distal joint of the thumb. The ovaries and tubes appeared normal for a child of the patient's age. The surface of the ovaries was smooth. A few follicles, showing beneath the surface, were apparently normal. The left suprarenal gland appeared normal. In the right suprarenal gland a circumscribed nodule occupied the space of the gland and was fixed to the kidney. The well-encapsulated mass was completely removed through an incision in the peritoneum in the right renal region. The vessels around the periphery of the mass were ligated without difficulty.

Pathologic report by Dr. C. A. Payne.—Grossly the specimen consisted of an adrenal gland (Fig. 3). The adrenal weighed 48 Gm. and

measured 5.5 by 4.5 by 3.3 cm. The gland was surrounded by loosely arranged connective tissue. The capsule was quite vascular. The gland contained an egg-shaped nodule which obliterated the normal contour and left only a thin rim of recognizable tissue. The tumor cut with moderate ease and presented a slightly bulging red-gray surface with many small, irregular, orange and yellow plaques distributed throughout the periphery. The tumor was fairly soft, apparently cellular, and quite vascular. Only small remnants of adrenal tissue were identified.

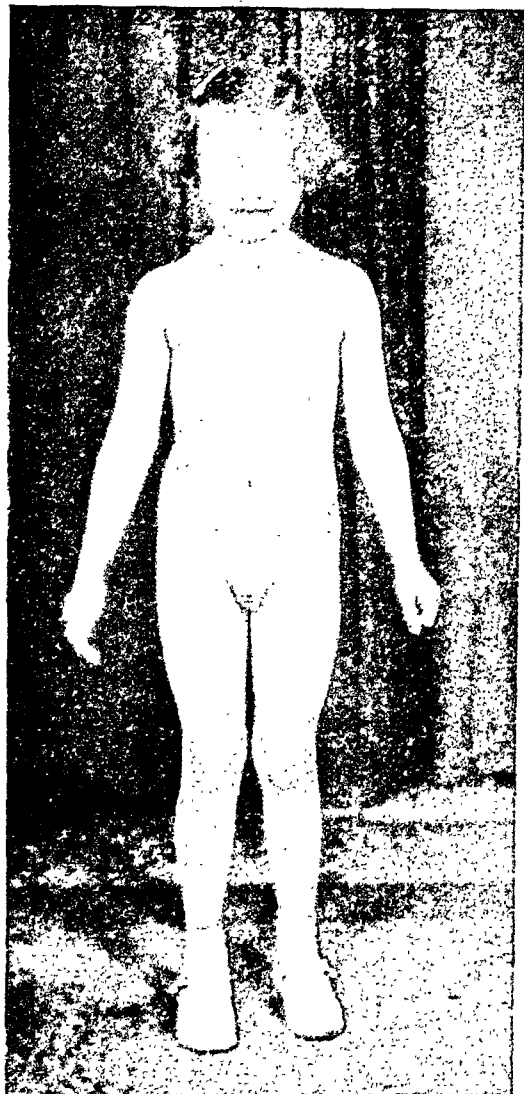


Fig. 4.

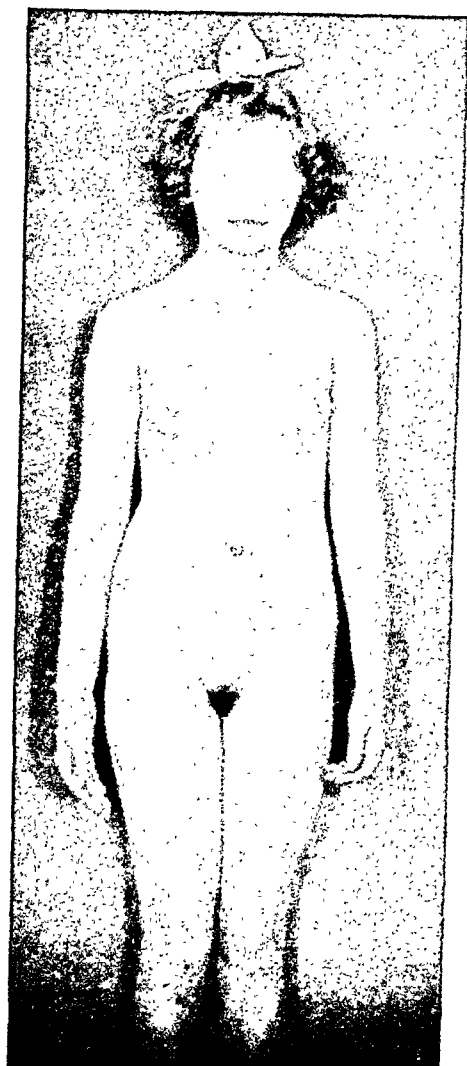


Fig. 5.

Fig. 4.—Case 1. One year after removal of tumor. Masculine trend diminishing.

Fig. 5.—Case 1. Taken at the age of 10 years. Shows feminine development in breasts and general contour of the body. Pubic hair only slightly increased.

Section through the tumor showed, in many areas, a rather definite fibrous capsule outside of which compressed and atrophic strands of cortical cells showing hemorrhagic infiltration were noted. The entire tumor was rather uniform in structure and was not unlike that seen in the normal adrenal cortex. The cells were of uniform size and shape and showed vesicular nuclei with varying degrees of chromatin and small nucleoli. The cells varied in size and shape but nothing suggested malignant degeneration. No mitotic figures were seen in the sections examined. The cells were arranged in strands and cords, and, in many areas, in definite adenomatous structures. Numerous sinusoids, many of which were filled with blood, were noted in the sections examined. Small areas of calcification and other areas of fibrosis were noted throughout the very scant stroma. Only small groups of the tumor cells pre-

sented a foamy or vacuolated cytoplasm similar to those noted in the normal adrenal cortex. The other cells had a rather deep staining eosinophilic cytoplasm which was slightly granular. Impression: Cortical adrenal carcinoma.

The postoperative course has been uneventful. Observations at intervals during six years have indicated no suggestion of metastases. The configuration of the body has been transformed to a more feminine type due to the relative increase of adipose tissue over muscular development (Figs. 4 and 5). Although the voice is still deep, it is less conspicuous than at the time of the operation, as has been determined by comparison of vocal recordings. The child's behavior is now characteristic of a girl of her age. The pubic hair remains unchanged. The labia and clitoris have diminished in size. The mucoid discharge has disappeared. There has been no progress in the growth of hair in the axillary or mammary region. The growth rate has returned to normal. Her measurements three years after the operation were as follows:

	ACTUAL	NORMAL VARIATIONS
Weight	58.0 pounds	39.2-48.8 pounds
Height	51.0 inches	44.2-47.2 inches
Span	51.0 inches	42.8-46.0 inches
Upper measurement	25.5 inches	23.0-25.0 inches
Lower measurement	25.5 inches	20.5-22.5 inches

Summary.—A girl, aged 2 years, 9 months, who showed marked signs of virilism, was operated upon and an encapsulated tumor in the right adrenal was removed. At the end of a period of six years there have been no signs of metastasis. There has been a marked reversal from the original picture to that of the normal female child.

CASE 2.—D. B., a female, aged 4 months when first seen, was born in April, 1935, and died May 15, 1937. She weighed 7 pounds at birth. Her physical and mental development was normal. She had fits of temper. Her appetite was excessive. At the age of 4 months a small tumor appeared on the left cheek close to the angle of the mouth. Thinking it was a blackhead, the parents squeezed it but obtained no secretion. A physician lanced the lesion but obtained only blood. The lump appeared at the age of 13 months as an ulcerated, fungating mass, 4 cm. in diameter. Biopsy taken May 19, 1936, was reported as follows: Gross examination: The specimen was a small piece of tissue 0.5 cm. in diameter. Microscopic examination: The specimen was a newly grown tissue with a slight fibrillary stroma. It was composed of cells which were highly anaplastic varying considerably in size, shape, and staining. In general they were spindle-shaped with some tendency to polygonal morphology. Many of them contained mitotic figures and a number of large multinucleated cells were present.

Following biopsy and x-ray therapy, the tumor receded, disappearing within four months. An indurated scar remained. Hair distribution increased, including heavy black hair on the head, a beard, and black pubic hair of the masculine type. The size and facial expression indicated an older child. The ears and nose were large. She had heavy bones and a large chest. Her voice seemed deep and husky. The clitoris and labia were overdeveloped. Hyperemia of the genitals was noted.

Laboratory procedures: Roentgenogram of the skull at the age of 15 months revealed a normal sella turcica. Roentgenogram of the chest showed a shadow, approximately 7 by 10 mm., in the region of the left hilus, suggesting a small gland. Osseous development in the elbows, knees, and pelvis was advanced from two to four years. A plain film of the abdomen gave no evidence of renal tumor. A Friedman test was negative. Fifteen hundred rat units of theelin per twenty-four hours were found in the urine.

In December, 1936 (age, 20 months), there was a recurrence of the lesion on the face. The hair development had increased. The voice was

even deeper. The larynx was prominent. The enlarged clitoris now suggested a phallus with hypospadias.

Roentgenogram of the abdomen showed a soft tissue mass the size of a fist in the left upper abdomen. It did not appear to be a spleen but suggested a lobe of the liver or an adrenal tumor.

Laparotomy Dec. 15, 1936, by Dr. A. J. Font: A right paramedian incision was made from 1.5 inches below the umbilicus to the symphysis pubis, and the peritoneal cavity was entered. The pelvic organs were explored and were found to be normal. On exploration the right kidney was found to be normal. Exploration of the left kidney revealed a palpable mass the size of a lemon in the region of the kidney. Due to the location of the incision, no further exploration was done and the abdomen was closed.

Laboratory tests following operation showed a normal nonprotein nitrogen, blood chlorides, blood sugar, blood calcium, blood phosphorus, blood count, and urinalysis.

Cystoscopic examination Jan. 7, 1937, by Dr. G. C. Burr: Inspection of the external genitals revealed a precocious development, particularly of the clitoris, which was greatly hypertrophied. As a result of this hypertrophy the urethra had the appearance of a hypospadias in the male. However, the urethra itself was normal and admitted a No. 16 French scope. The urine was clear and the bladder was normal throughout. The right and left ureteral orifices were normally placed and functioning. The urine from each kidney was clear. A pyelogram was made of the right side and then on the left side. Inspection of the roentgenogram revealed a normal kidney on the right side. The calyces were stretched out in the upper portion of the left kidney, suggesting involvement of that portion of the kidney in the tumor mass. This, however, was not marked and the kidney might well be normal in its entirety. Diagnosis: Precocious sexual development and adrenal tumor.

After the laparotomy, pus drained from the wound for four weeks. Temperature reached 104° F. In late January and early February, 1937, deep x-ray therapy was applied over the tumor of the cheek with no apparent effect. In April the patient complained of severe pain in her hip. The lesion on the face had enlarged. Metastases had appeared in the left lung, the cheek, and the bones. She failed rapidly and died May 15, 1937, at the age of 25 months.

Microscopic examination of the tumor obtained at autopsy: The tumor tissue of the left adrenal, lungs, pleura, cranium, and neck was found to be of the same structure. Likewise, it was found to be identical with the biopsy of the lip lesion which was made a year previously. The tumor tissue was composed of a variety of cells which varied greatly in size, shape, and staining. Most of them were large and contained large nuclei. The staining of the nuclei varied greatly, some of them being hyperchromatic and others staining poorly. Some of the cells were multinucleated. The cytoplasm was abundant, nongranular, and stained poorly. The cell borders were indistinct. There was no differentiation into glands and no adrenal zones were being produced. The stroma was scanty and fibrillary. Microscopic examination of the metastatic processes showed a similar picture. The anterior lobe of the pituitary gland contained an abundance of alpha or acidophil cells. The liver and spleen exhibited a moderate engorgement of the vascular system, otherwise no pathology. The ovaries exhibited a large number of follicles: some were immature and some were nearly mature. There were a number of poorly formed corpora albicantes. Section made through the base of the clitoris revealed large corpora cavernosa.

Summary.—A female child at 4 months of age presented signs of virilism which increased until near her death at the age of 25 months. The first lesion noted was fibrosarcoma of the cheek. This metastasized to the left adrenal which accounted for the signs of virilism. The death of the patient was due to the malignant tumor of the cheek and its

metastases. The virilism appeared as a consequence of metastases to the adrenal.

CASE 3.—D. B., a female, showed virilism and retarded growth. Her age was 8 years, 4 months Nov. 19, 1938.

Developmental history: The patient's birth weight was 6 pounds, 2 ounces. The mother's endocrine response to the pregnancy was normal. Other developmental advances, such as walking, talking, and teething, were entirely normal. There were no complaints until the age of 5 years, at which time failure to grow was noted. There had been a growth of only two inches in the previous two years. At the age of 7 years, pubic hair was first noted, and since that time an increase in length and number had been evident. Increased growth of hair on the arms and legs was noted. The child was precocious and in an advanced group at school. The parents revealed that excessive strength had always been present. She had always been "tomboyish," being an excellent trapeze performer. Both the family and past history were essentially negative.

Physical examination:

	ACTUAL	NORMAL VARIATIONS
Weight	48.0 pounds	48.6-60.6 pounds
Height	43.5 inches	48.2-51.6 inches
Span	45.0 inches	47.5-51.1 inches
Upper measurement	23.5 inches	24.4-26.6 inches
Lower measurement	20.0 inches	23.4-25.6 inches

The child was moderately well nourished. Musculature was excessively developed and of the male type. This was especially true of the muscles of the upper legs. An excessive hair growth was noted on the arms, legs, and lumbosacral region. There were approximately thirty or forty black pubic hairs on each side, measuring one inch in length. There were no signs of voice change, axillary hair, or breast development. The labia were enlarged. The clitoris was well formed.

Laboratory procedures: The following laboratory tests were done and all were found to be entirely within normal limits: urinalysis, complete blood count, blood sugar, blood nonprotein nitrogen, blood calcium, blood phosphorus, Kahn, basal metabolism. Blood cholesterol was increased, being 241 mg. per 100 c.c. of blood. This test was repeated after two days and the amount was 230 mg. per 100 c.c. of blood. Bio-assay of the urine was negative for estrogens and androgens.

Roentgenogram of the skull revealed a normal sella turcica. Roentgenogram of the chest for thymus was normal. X-ray of the abdomen revealed no abnormal shadows in the adrenal area. Roentgenogram, following air injection in the adrenal area, did not reveal signs of abnormal shadows. X-ray study for osseous development revealed an advance of one to two years.

Course: On Jan. 5, 1939, at the age of 8 years, 6 months, an exploratory operation was done. The uterus was found to be small for a child of the patient's age. The tubes were normally developed. The ovaries appeared to be normal, about 0.20 cm. in length. The surface was smooth. Five or six pink follicles showed through the surface, but there were no visible corpora lutea. There was no enlargement of the adrenals. No physical findings at the exploratory operation explained the sex precocity.

The patient was last seen Aug. 7, 1940, at the age of 10 years, 1 month, and the following measurements were recorded at that time.

	ACTUAL	NORMAL VARIATIONS
Weight	60.0 pounds	56.2-71.0 pounds
Height	47.0 inches	51.2-54.8 inches
Span	48.0 inches	50.7-54.5 inches
Upper measurement	25.0 inches	25.5-27.9 inches
Lower measurement	22.0 inches	25.1-27.5 inches
Chest	24.0 inches	25.0 inches (optimal)
Abdomen	22.0 inches	21.8 inches (optimal)

Examination revealed that there had been a slight but definite increase in pubic hair. The breasts still showed no signs of development. An occasional axillary hair was noted. The musculature and build were still of the masculine type.

The mother reported that the masculine tendencies decreased and the femininity increased.

Summary.—This girl, aged 8 years, 4 months, displayed signs suggesting virilism. Adrenal tumor was suspected, but exploratory operation revealed no adrenal enlargement. The discrepancies, when compared with the other two patients, were lack of increased statural growth, no change in voice, and only moderate enlargement of the clitoris. Her behavior was masculine.

Discussion

The clinical manifestations of the three cases vary considerably, but the factors common to all of them are symptoms appearing in early childhood; all females; premature sexual development; virilism; rapid growth; evidence of disturbance of adrenal function; normal gonads, and lack of evidence of tumors in the region of the third ventricle or pineal gland; no increase in androgens or estrogens.

Pseudohermaphroditism was eliminated from the diagnosis because the children were normal at birth. In Case 1 the adrenal tumor might have been present at birth, though no symptoms indicated it until the third year of life. In Case 2 the metastatic tumor in the adrenal could not have preceded the visible lesion on the cheek discovered at the age of 4 months. In Case 3 the time of increased adrenal activity remains indefinite, the signs of virilism were less conspicuous, and the diagnosis of virilism may be questioned.

Sex precocity is more frequent in the female. All of our patients were females. In a previous report by one of us (R. L. S.) females predominated.

The age at which functioning sexual organs developed varies widely. The accepted average of 13 to 14 years is computed from a wide range. One hesitates to state the earliest age at which sexual development may be considered normal, but he may be guided in the individual problem by comparing general body development and function. In the three cases reported, sexual development may be considered premature because it is not proportional to the other structures and functions. Prematurity was manifested by the rapid development of the genitals, rapid growth, and osseous development.

Virilism in the female signifies sex reversal and is comparable with sex precocity in the male. It was manifested in all three patients by change of voice (most conspicuous in the patient in Case 1), hirsutism, enlarged clitoris, masculine contour, and masculine behavior. Accepting the criteria for diagnosing virilism as the appearance of at least two of the signs (change of voice, enlarged clitoris, and hirsutism), the patients in Cases 1 and 2 qualify. In the third patient (Case 3) hirsutism was conspicuous, the enlargement of the clitoris was only moderate, and the voice was not changed. In retrospect, this patient should have been observed longer before operation was advised. Negative findings in the adrenal and ovary facilitated the subsequent treatment.

Regarding the operative approach to a suspected adrenal tumor, the abdominal incision offers several advantages. By the lumbar route,

both sides must be opened to locate the tumor, to insure that one adrenal is normal, and other viscera cannot be explored. A small incision at the level of the umbilicus permits exploration to determine the location of the lesion. If an arrhenoblastoma is found in an ovary, the incision can be extended downward to expose the ovary satisfactorily. If an adrenal tumor is found, the incision may be extended upward and the adrenal can be satisfactorily approached. Thorough exploration affords valuable information that would be lost if the lumbar route were used.

Mild degrees of virilism are not uncommon, but among all of those observed, only the two reported herein have been definitely associated with adrenal tumor. The series is too small to permit assuming definite criteria for the differentiation of virilism with and without adrenal tumor. My impression at present is that those with tumor tend to progress steadily and more rapidly than those with a milder type of virilism. It is hoped that as more cases accumulate in the literature, the means of preoperative diagnosis will become more accurate.

Discussion

DR. J. P. GREENHILL, CHICAGO, ILL.—At the present time the subject of pubertas praecox or sex precocity is in a state of confusion. In many cases of sexual precocity the etiology can be detected and removed, but in a large number the cause cannot be found except at autopsy. Some cases are associated with signs of virilism such as the ones reported by Pratt, but in most instances of sex precocity virilism is absent. Likewise, whereas adrenal tumors were present in Pratt's cases, the majority of cases of pubertas praecox have no involvement of the adrenal gland.

A survey of the literature reveals numerous case reports and a few reviews of the reported cases with attempts at classification and explanation. There is no semblance of unity concerning the total number of cases reported. One author¹ maintains that more than 500 cases have been reported, whereas only four years previously two other authors² were able to collect only eighty cases from the literature. According to Dennis, premature puberty is preceded and accompanied by an acceleration of skeletal development and of ossification. Therefore children who have reached puberty at a very early age are far above the age standards in respect to all body measurements. Their bodily proportions resemble those of the adult, but the development of their nervous system seems unaffected by these changes and is compatible with their chronological rather than their physiologic age. A study of twenty-five children who reached puberty before 2 years of age revealed that they did not walk earlier than other children. Of Keene and Stone's collected eighty cases of all types of pubertas praecox, 60 per cent were girls.

The causes of sex precocity may be divided into the following four groups:

1. Those associated with adrenal tumors like the cases reported by Pratt. In this group there are more females than males. Most of these cases have associated virilism, such as hirsutism, enlarged clitoris, and marked muscular development.

2. Those due to ovarian tumors. Various types of ovarian neoplasms have been encountered including malignant teratoma and carcinoma, but in most cases the tumor is of the granulosa-cell or of the theca-cell type. Young girls who have granulosa-cell tumors menstruate but they do not ovulate; hence they cannot become pregnant. Lull³ claims that only sixteen cases of ovarian tumors have been reported in very young children who showed signs of precocious puberty. He reported two cases of his own.

3. Those associated with lesions of the brain. This is a heterogeneous group because it includes cases of pubertas praecox associated with ventricular cysts, tumors of the tuber cinereum, tuberous sclerosis of the brain but especially hydrocephalus and disturbances of the hypophysis and pineal body. Among 177 cases of pineal body tumors collected from the literature by Bing, Globus, and Simon⁴ there were

twenty-one cases of *pubertas praecox* but only one was in a female. Dorff and Shapiro⁵ suggested that chronic increased intracranial pressure with compression of the hypothalamic-infundibular-hypophyseal pathway is the starting point of the development of the precocious state. Kraus, quoted by Dorff and Shapiro,⁵ maintained that in patients with neoplasms of the brain and meninges and in patients with chronic hydrocephalus associated with chronic increases in intracranial pressure, the anterior lobe of the pituitary gland becomes either overactive or underactive, depending on the particular changes that have occurred in the hypothalamic region. In 83.3 per cent of Kraus' cases with increased intracranial pressure, the ovaries showed microcystic degeneration. In 60.3 per cent the follicle-stimulating hormone was increased in the blood and urine. Some patients gave positive Aschheim-Zondek tests. In the group of cerebral lesions Novak includes Albright's syndrome which consists of disseminated fibrosis of the bone, extensive patchy, cutaneous pigmentation, precocious growth and (in females) precocious puberty. Albright⁶ found the ratio of females to males to be 3:2. Up to 1934 thirty-four cases of Albright's syndrome had been reported in the literature.

4. The *constitutional type* named and graphically described by Novak.⁷ I agree with Novak that this is the most common type of precocious puberty. These patients develop a very early puberty without detectable disturbances in any endocrine gland or any organ of the body. Novak believes that the reason these children skip part or all of their childhood is that there is a disturbance in certain genes. The remarkable facts about the constitutional cases of precocity are that the children remain healthy and live on as do the girls who begin puberty at the customary times and they not only menstruate but also ovulate at least soon after the menses are well established. Therefore they are capable of becoming pregnant at an early age. I further agree with Novak that all the cases of pregnancy which have been reported in girls from 5 to 9 years of age have occurred in constitutional cases of sex precocity. While great interest is centered in the group of constitutional cases by the parents, siblings, relatives, and doctors during their early childhood, after the age of 10 or 11 these youngsters do not differ from the girls who have had their puberty at the proper time.

Of what practical value is this knowledge of the classification of the causes of sex precocity? The most curable group is that due to granulosa-cell and theca-cell tumors, but such cases are very rare. In most of these cases removal of the ovarian neoplasm results in cure, but we must remember that these tumors are malignant. The second group of cases where at least some of the patients may be restored to their normal sex status is the type associated with adrenal tumors. Hence in cases where no ovarian tumor is palpable and certainly when signs of virilism, particularly hirsutism, are present, it is justifiable to perform an exploratory operation in the hope of finding an adrenal tumor. The most hopeless cases are those in which there is a lesion of the brain. Even if a correct diagnosis can be made before death, the prognosis is grave.

In the constitutional group of cases no treatment can be carried out to overcome the sex precocity. However, since the secondary sex characteristics of these youngsters make them attractive to mature boys and adult men, they must be carefully guarded against coital indulgences. Not only are there dangers of venereal infection and psychic effects, but also risk of pregnancy because these children ovulate in contrast to the cases in the other groups. Since sex precocity is more common than is generally believed, we as gynecologists should acquaint ourselves with the available knowledge of this subject so that we can cooperate with the pediatricians and parents in the care of these children.

References

1. Dennis, Wayne: *Am. J. Dis. Child.* 61: 951, 1941.
2. Keene, C. M., and Stone, C. P.: *Psychol. Bull.* 34: 123, 1937.
3. Lull, Clifford B.: *Am. J. Obst. & Gynec.* 41: 445, 1941.
4. Bing, J. P., Globus, J. H., and Simon, H.: *J. Mt. Sinai Hosp.* 4: 935, 1938.
5. Dorff, G. B., and Shapiro, L. M.: *Am. J. Dis. Child.* 53: 481, 1937.
6. Albright, F., Butler, A. M., Hampton, A. O., and Smith, P.: *New England J. Med.* 216: 727, 1937.
7. Novak, Emil: *Am. J. Obst. & Gynec.* 47: 20, 1944.

DR. EMIL NOVAK, BALTIMORE, MD.—The distinction which gynecologists most frequently must make in these cases of precocious puberty is between that of the granulosa-cell tumor variety and that of constitutional type. The other possible causes are, as a rule, readily eliminated, sometimes almost at a glance. For example, in the adrenal cases, such as those reported by Dr. Pratt, a precocious puberty characterized by heterologous sex characters is exhibited. They show hypertrichosis, but the hair growth involves not only the genitals and axillae, but usually other parts of the body, like the abdomen or extremities, with at times tufts of hair on the back. In the granulosal and constitutional cases, on the other hand, the hair is apt to be limited to the genitals and axillae, just as it is in the girl at normal puberty.

Again, in the adrenal cases there is often marked hypertrophy of the clitoris, which is never seen in the constitutional or granulosa-cell tumor cases. Finally, the precocious development seen in the adrenal cases is associated in only a minority of cases with precocious menstruation, a characteristic manifestation in the other two chief varieties.

The pineal tumor group, the tumor usually being a teratoma, does not concern the gynecologist, since, with one possible exception, all known instances have occurred in males. Furthermore, the precocious changes are probably due to involvement of certain brain areas rather than of the pineal body itself. Other causes of precocious puberty, such as tumors of the hypothalamic areas, are commonly characterized by definite cerebral symptoms far graver than the precocious sex changes.

The granulosa-cell tumor variety presents changes like those we might expect from the administration of large amounts of estrogen to infants or young children, and the menstrual bleeding which they show is purely estrogen-induced and not of course associated with ovulation. In this important respect they differ from the far more common cases of constitutional or genic type, in which ovulation does not occur, and precocious pregnancy is therefore possible. Unless one can actually palpate an enlargement in one or other ovary, one should lean toward the latter diagnosis. Dr. Greenhill has kindly alluded to my recent publication on this subject in which a report was made of nine such cases which I have observed. Another instance has been encountered since the publication of this paper.

HABITUAL ABORTION*

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THE inability of a woman to pursue a pregnancy to its fruition, the birth of a child which has a chance of survival, is of importance not only to the individual involved but also to a nation whose birth rate is low. To the individual, a repetition of this accident several times is a keen disappointment bordering on the tragic, and in her physician it creates a sensation of frustration and of his inadequacy. Taussig says: "How much human happiness is involved in the saving of these fetal lives! What greater triumph than to bring to pass the birth of a living child by a mother who for years has had her hopes thwarted by habitual abortions!"

The causative factors of repeated abortions are not well understood, but, according to present ideas, might be summarized in three groups:

1. *Maternal.* a. *Pelvic Organs.*—Malpositions, tumors, infections, lacerations of the cervix, and an endometrium incapable of proper decidua formation permitting satisfactory nidation.

*Read at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1914.

b. *General*.—Syphilis, toxic agents such as alcohol, lead, and phosphorus, anemias, dietetic deficiencies (avitaminosis), and endocrine disturbances; under this last heading can be included hypothyroidism and hyperthyroidism, and deficiencies or imbalance of estrogen and corpus luteum, and possibly blood incompatibility between the husband and wife. We may yet learn that there exists a condition similar to the Rh factor responsible for erythroblastosis.

2. *Paternal*.—Excessive sexual activity or sexual exhaustion. Infections: syphilis, gonorrhea, prostatitis. Endocrine disturbances: hypothyroidism and hyperthyroidism.

3. *Ovum*.—A condition of the ovum incompatible with its continued uterine life; this has been called defective germ plasma. Hertig and Edmonds found abnormal ova in 47.4 per cent of 53 consecutive cases of spontaneous abortion. Whether these abnormal ova are due to abnormalities in the germ cells or to developmental environment such as an unhealthy decidua is unsettled. It is possible that either or both may be operative. If this is true, it would seem that the latter might be susceptible of correction.

Management

Prior to the present treatment of repeated abortions, the care of this condition was limited to months of absolute bed rest. This was often ineffectual and women aborted during long periods of such immobilization.

The husband and wife should be subjected to as painstaking investigation as that undertaken in the diagnosis of sterility. There is a correlation between these two conditions. Women infertile because of ovarian failure, who later conceive, often abort due to the cause of their sterility. Appropriate treatment should follow the discovery of any possible causative factors. The correction of a retrodisplaced uterus is best done before conception with the fitting of a pessary. Too much manipulation of a pregnant uterus may defeat our object. In the majority of cases, however, no local causes are found, and the management resolves itself into measures aiming to correct deficiencies of endocrines and vitamins. The patient should be instructed to refrain from exertion on the days of her first four missed menstrual periods. Intercourse should be interdicted for four months. The entire subject should be carefully explained to her; she should be encouraged, but no absolute promise of success should be given. Because of the intense desire for children, these patients are usually cooperative.

Progestin by intramuscular injection, 5 units every four days, is begun after the first missed period. In case of any bleeding or pelvic pain she should be put to bed and the frequency of the progestin injections increased. Morphine is not indicated, but simple sedatives can be used. Peroral administration of anhydrohydroxyprogesterone offers a more convenient method of therapy. Hamblen believes it to be as efficient as the intramuscular injection of progestin. Soule, Krohn, and Greenblatt concur in this. Still another method should, because of its simplicity and economy, receive further trial, that of pellet implantation described by Mishell. Interruption in the third trimester of pregnancy initiated by contractions or rupture of the membranes may be due to the preponderance of estrogen. Progestin is indicated and may act as an antagonist to prevent premature labor.

Results

Of the 30 patients treated, 28 delivered living, normal children, 22 at full term and 6 between 7½ and 8¾ months.

TABLE I. RESULTS IN THIRTY CASES OF HABITUAL ABORTION TREATED WITH PROGESTIN

NO.	LENGTH OF PREVIOUS PREGNANCIES IN MONTHS	WEEK TREATMENT BEGUN	WEEK TREATMENT STOPPED	ABORTION THREATENED THIS PREGNANCY*	WEEK THREATENED	RESULTS
1	3	4	17½	P	10	9 mo. normal child
2	3½, 9, 9, 1½, 3	8	35	P and H	9	8½ mo. normal child
3	9, 9, 2, 3	14	16	P	12	9 mo. normal child
4	4½	5	26	H	13	9 mo. normal child
5	9, 9, 9, 3	8	15	P and H	9	9 mo. normal child
6	9, 8, 2½, 3, 3, 2½	7	21			9 mo. normal child
7	9, 7	5	35	P	6 and 31	8½ mo. normal child
8	9, 4, 3½, 9	5	9	H	7	9 mo. normal child
9	5, 8, 8	6	31	P and H	12	8 mo. normal child
10	3, 3, 3	5	33	P	5	9 mo. normal child
11	4½	7	28	P	8	9 mo. normal child
12	4, 9, 2, 3	5	16	H	7	9 mo. normal child
13	9, 2½	7	14			9 mo. normal child
14	3, 4½, 3, 3½	5	16	P and H		4 mo. aborted another
15	9, 9½, 3½, 3½, 3½, 3½, 3½	10	17			9 mo. normal child
16	1½, 2	5	23	H	16	8½ mo. normal child
17	5, 9, 2, 4	7	21			9 mo. normal child
18	2½, 2½	6	34	P	25	9 mo. normal child
19	7½, 4½	5	16	H	5	8½ mo. normal child
20	2½	7	17	P	14	9 mo. normal child
21	8, 9½, 3	3	17			9 mo. normal child
22	2, 3½, 9, 2	5	26			9 mo. normal child
23	9, 5, 9, 2	4	12	P and H	5	9 mo. normal child
24	2½, 3½, 2	5	15	P	6	9 mo. normal child
25	9, 2, 2	4	25	P	17	9 mo. normal child
26	9, 9, 2, 3½, 2	6	24			5 mo. missed abortion
27	9, 2, 2, 3	4	26			9 mo. normal child
28	3, 3, 3	6	32			8½ mo. normal child
29	4	6	30			9 mo. normal child
30	9, 3, 4	11	30	P and H		7½ mo. normal child

*P = Pain.

H = Hemorrhage.

TABLE II. COLLECTED RESULTS IN PROGESTIN THERAPY IN HABITUAL ABORTION

AUTHOR	CASES	FAILURE	SUCCESS	PER-CENTAGE SUCCESS
Kotz, Parker, and Kaufman (collected cases)	273	57	216	
Kotz, Parker, and Kaufman (own cases)	42	5	37	
Davis, Hamblen, Cuyler, and Baptist	24	8	16	
Mason, L. W.	19	2	17	
Quigley, J. K.	30	2	28	
Total	388	74	314	80.9

One failure, Case 26, was that of a woman whose first two pregnancies terminated at term uneventfully, but whose third, fourth, and fifth pregnancies resulted in spontaneous abortions at between two and three months. During her sixth pregnancy she received progestin from her sixth to twenty-fourth week, when she had a missed abortion of a three and one-half to a four months' fetus.

Another patient, with a history of four previous abortions and no living children, aborted at the fourth month and since then has had the same experience under the care of another physician, making her sixth abortion, all occurring at the end of the fourth month. Five patients required progestin to prevent the onset of labor at seven months; three of these delivered in the ninth month and two at full term. Early threat to abort was common in this series; five had hemorrhage only, none had pain only, and five had pain and hemorrhage.

Of those cases having had only one previous abortion, two had been treated for sterility, a condition akin to habitual abortion and in which abortion can be predicted. The others were included for two reasons: symptoms of abortion in the present pregnancy, or previous premature labors. Uterine curettement was done in three cases of this series in the hope that an endometrium would result more favorable to nidation. Four having metabolism rates below normal were given thyroid extract. All cases received progestin by intramuscular injection in doses varying from 1 to 5 units every three or four days.

The incidence of habitual abortion is not high; the number of cases reported by one physician from his own experience is limited. For this reason, I have collected the published experience of many others who have employed progestin prophylactically.

Discussion

The object of this report is not to contribute anything new to the understanding of this condition, but to briefly review a series of cases which were treated successfully, it is believed, by a method which had received wide acceptance, but which recently has been challenged. Taussig in his book *Abortion* says: "No method of treatment for the prevention of abortion has been attended with as much success as that of endocrine therapy." It is true that much of the criticism of this therapy has been directed against its employment in threatened abortion rather than prophylaxis against habitual abortion; nevertheless, the principles upon which it is founded apply to both conditions. Paine questions the validity of the experiments by Moir to prove the sedative effect of progestin upon the uterine musculature. This assumes that the only function of the corpus luteum is to prevent uterine contractions, ignoring its action in favoring nidation. Aside from laboratory evidence progestin is known to relieve afterpains and false labor pains (painful Braxton-Hicks contractions), both due to uterine contractions. Hamblen, after pregnanediol determinations in pregnant women, concludes as a result of these observations that the administration of progestin is not indicated. "Any beneficial effect, which therapy with progesterone possesses in the treatment of habitual abortion, cannot be explained upon the basis of its complementing deficits in progestin pregnanediol metabolism."

Proof of the sedative effect of progestin upon the uterus is not adduced here except in a clinical manner. Krauss, Moir, and others have demonstrated this by the intrauterine use of the bag.

Coincidence might be cited as a reason for the birth of living children to women who had previously had from two to five spontaneous abortions; in other words, these pregnancies untreated would have pursued a normal course. The results in at least twelve of these cases were too striking to admit of this explanation. Aside from this, two of these women subsequently tried to go through the term without treatment and failed.

It has been claimed that the rest prescribed for these patients might be the therapeutic factor. Two arguments against this are: First, it was minimal. The only bed rest advised was for a part of the time each day of the first three missed menstrual periods and not all of

them had even that. Second: We all have seen women, on absolute bed rest for four or five months, abort while in bed.

Objection to the prevention of habitual abortion has been raised on the ground that abortion is Nature's method of disposing of imperfectly formed fetuses, and therefore the preservation of pregnancy should not be encouraged. There is, of course, this possibility, a risk which must be taken. There is much evidence in favor of an increased percentage of fetal abnormalities in children born at term after threatened abortion early in pregnancy. This tendency probably does not exist to the same degree in habitual abortion as in threatened abortions. Fortunately there were no abnormal children in this small series. Had this fear been acted upon, few of these twenty-eight couples would probably have children today. Another objection is that of the cost of the substances employed. Were this compared to the expense involved in the adoption of a baby, it would be insignificant, and most women prefer a child of their own. One more criticism is that this plan does not always succeed. Is there any therapeutic measure that is infallible? Absolute promise of success should never be made, but even a 50 per cent chance would be accepted by most women.

The only cases of threatened abortion here reported are those cases of habitual abortion under prophylactic treatment where hemorrhage or pain or both occurred. The threat in all but two of these subsided and they went on to term resulting in the birth of normal children.

The prophylactic treatment of repeated abortions instituted as soon as pregnancy is diagnosed is quite a different matter from the treatment of threatened abortion. Both Mall and Hertig have shown that approximately 50 per cent of all early abortions are due to fetal fault or imperfection. It is also known that fetal death antedates by days or weeks the onset of symptoms in many cases. From this we can conclude that treatment by rest, sedative, progestin, or any other means does not offer as much hope of success as treatment begun before the appearance of symptoms.

To determine the viability of the early fetus, Rutherford does an aspiration biopsy of the decidua of the lower uterine segment and says that the normal viable fetus is not apt to be expelled by the instrumentation involved. There should be some hesitancy in adopting this diagnostic procedure in the repeated abortion case where little manipulation is needed to inaugurate hemorrhage or contractions or both.

Conclusions

1. Twenty-eight of the thirty women who were habitual aborters under treatment went to full term or near it, and gave birth to normal children.

2. Uterine curettage was done in three cases, and in four cases thyroid extract was given.

3. Successful termination of a pregnancy treated prophylactically against abortion does not guarantee full term in a subsequent pregnancy untreated.

4. Two possible fields for further investigation as to the cause of repeated abortions are: (1) The quantitative relation between the

estrogen and corpus luteum secretions. (2) Blood incompatibility of husband and wife similar to the Rh factor in erythroblastosis.

5. While there is some question from experimental evidence as to the value of progestin to prevent abortion, the writer feels that the results reported by many careful observers warrant its continued use at least until a better method is evolved.

References

- Taussig, F. J.: Abortion, St. Louis, 1936, The C. V. Mosby Co., p. 117.
 Hertig, A. T., and Edmonds, H. E.: Arch. Path. 30: 260, 1940.
 Soule, S. D.: AM. J. OBST. & GYNEC. 42: 1009, 1941.
 Krohn, L., and Harris, J. M.: IBID. 41: 95, 1941.
 Greenblatt, Robert B.: Bull. Univ. Hosp., Univ. of Georgia, March, 1941.
 Mishell, Daniel R.: AM. J. OBST. & GYNEC. 41: 687, 1941.
 Kotz, J., Parker, E., and Kaufman, M.: J. Clin. Endocrinol. 1: 838, 1941.
 Davis, C. D., Hamblen, E. C., Cuyler, W. K., and Baptist, M.: Ibid. 2: 377, 1942.
 Mason, L. W.: AM. J. OBST. & GYNEC. 44: 630, 1942.
 Paine, A. K.: Bull. New England M. Center 5: 33, 1933.
 Hamblen, E. C.: AM. J. OBST. & GYNEC. 41: 664, 1941.
 Knaus, H.: In Corner, G. W.: The Hormones in Human Reproduction, Princeton, 1942, Princeton University Press, p. 122.
 Mall, F. P., and Mayer, H. W.: Carnegie Inst. Was. Publication No. 275, p. 3.
 Rutherford, R. N.: Surg., Gynec. & Obst. 74: 1139, 1942.
 Moir Clinic, Brit. M. J. 1: 1022, 1932.

Discussion

DR. A. K. PAINE, BOSTON, MASS.—Dr. Quigley frankly states that his employment of progesterone was based on numerous published reports of its successful use in the treatment of habitual abortion. Because he entered into no extended discussion of the rationale of progesterone therapy in such cases, discussion perhaps could properly be limited to case reports, in general and in particular.

A review of thirty-six articles on habitual abortion discloses an interesting variety of therapeutic agents. Exclusive of the usual bed rest, sedatives, etc., the list includes the progesterones, vitamins E and K, thyroid, placental extract, anterior pituitary-like hormone, estrogens, pregnancy serum, sodium iodide, and organic arsenicals. Exclusive of the progesterone series, the average success rate of this intriguing therapeutic display was approximately 80 per cent. Progesterone on the other hand, used alone or in various combinations, even though some authors reported a 100 per cent success, curiously had an average success rate of only 74.5 per cent.

The extract of corpus luteum series is not included in these progesterone percentages because of some question as to whether it represents a source of the latter, or something else.

As long as results are satisfactory, it is probably captious to wonder about combinations of therapeutic agents, progesterone with vitamin E, thyroid, etc., and to which in such instances the success should be credited. We are thankful that in Dr. Quigley's cases this question arises infrequently. Three had a prior curettage. Most of us, I suspect, would be glad to give full credit to the progesterone, hoping thereby to forget that not so long ago a prior curettage was a *sine qua non* in the treatment of habitual abortion. But what of the four cases with an accompanying thyroid therapy? We have been repeatedly reminded of the importance of thyroid dysfunction in these cases, and White reports a 90 per cent success with thyroid extract.

Studying case reports, one is conscious of another insistent question, rather sophomoric perhaps, but what is meant by the term habitual abortion? Hertig suggests that a patient should have at least *two* prior consecutive spontaneous abortions before she can be termed an habitual aborter. Javert and Stander recently stated that their criterion was *three* prior consecutive abortions. Is not something involved here beyond a mere academic interest in terminology from the standpoint of dependable statistics? Many reported series with high success rates include cases which have had but one previous abortion.

A pregnancy with a history of a previous abortion, premature delivery, or a long period of sterility certainly furnishes reason for considerable anxiety and

the physician is justified in employing procedures he believes may minimize unfortunate possibilities. When such a pregnancy terminates successfully, it is natural perhaps to assume or believe that, without the specific treatment, the patient would have aborted. If she had aborted, she would then be an habitual aborter. But the use of such intangibles and the assumptions based thereon to attest statistically the value of some treatment is open to a good deal of question. It stands to reason that success percentages will be measurably higher if cases are included as such, which are not in fact repeated aborters.

There also appear frequently in reports of some highly successful treatment for threatened abortion numerous cases which *did not have* the most common, characteristic, and usually the *first* symptom of threatened abortion, namely bleeding. Dr. Quigley is to be commended for excluding this questionable group from his series.

We have at present no convincing evidence that all or any habitual abortions result from a progesterone deficiency, nor have we any definite evidence that progesterone administration will correct such a deficiency if it exists. On the contrary, such evidence as we have, Hamblen's work for instance, seems to indicate it will not.

The empiricism which progesterone therapy at present represents could well remind us that for a time, based on successful case reports, an early commercially available anterior pituitary-like hormone was also widely exploited as a last word in the treatment of habitual abortion.

DR. FREDERICK H. FALLS, CHICAGO, ILL.—In 1934 when we began to get interested in progestin, one of the drug companies went to considerable expense to produce what was called "corlutin" which was standardized by the use of the virgin rabbit's uterus. Two of my associates and I started to use it. We soon began to see that in women who were beginning to abort and received these injections, something happened. In about 1934 we reported forty cases, some of which were habitual abortions, with a very much higher percentage of salvage than any of us had seen. We had 86 per cent salvage in a group of women who had had 85 per cent failures in previous pregnancies.

About the following year I began some studies with an intrauterine bag which was inserted into a seven-day puerperal uterus connected to a kymograph. I injected an ampule of pituitrin which was followed immediately by uterine contractions. I waited for about five minutes to get these contractions well established and then I injected some of this "corlutin." The uterine contractions within five minutes stopped and remained so for about twenty minutes. I used another ampule of pituitrin and another and they did not start again. I drew the conclusion that this material inhibited contractions of the uterus produced by the posterior lobe pituitary extract. For the first time I felt that the clinical results we had obtained had a foundation that could not be ascribed to wishful thinking.

The expense of the oily preparation was too great and we wondered whether the cheaper, watery suspension of the corpus luteum had this contraction inhibiting material in it. We used the watery extract and found that by using more of the extract (about 10 to 1) we got practically the same response. When we first began to use the oily extract it was furnished to us in $\frac{1}{25}$ of a rabbit unit. We asked for a more potent ampule and they made $\frac{1}{10}$ of a unit and with that we got better results. Then we thought that about 1 c.c. of the watery extract would be about equal to the $\frac{1}{10}$ unit of the oily preparation. So we continued our experiments using larger volumes of the extract of the corpus luteum, we found that we got good results with the watery extract and that the cost to the patient was less.

We then collected a series of close to 500 cases of threatened abortion in the County Hospital and the Research Hospital and in one private practice. We found that the salvage from abortion amounted to about 85 per cent in the three groups. Then we stopped using the lutein extract at the County Hospital but treated the patients otherwise exactly as before. We found that the salvage dropped to only about 40 per cent. Then we went back to the injections and found that we got the same results as before.

Our conception of the value of this material is therefore based on clinical experience, and on the evidence that by the use of both the aqueous and the oily extractions of corpus luteum you can stop human uterine contractions stimulated by pituitrin. We feel that these contractions are an important factor in the mechanism

of abortion. Fifteen per cent of the cases still aborted and I think that will always be true. I do not think any one can every stop abortion cases 100 per cent.

This report of Dr. Quigley is exactly what one would expect if he has had any experience with this treatment in this condition. All over the country, men are using this material and with very good results. Personally, my mind is made up on the basis of what I have told you. Both clinically and in the laboratory this material gives results that I have not seen in the treatment of habitual or threatened abortion when it is not used.

DR. WILLARD R. COOKE, GALVESTON, TEXAS.—About twenty-four years ago I reported a series of seventeen cases of what we considered true habitual abortion. In this series, all of the patients were found to have hypothyroidism. All were put on adequate doses of thyroid extract and fourteen of the patients went through to term. Two promptly aborted within two weeks after they had voluntarily stopped taking thyroid. One of these two later continued the treatment throughout pregnancy and was successfully delivered. Several of these and subsequent patients have had more than one baby while on thyroid therapy. It goes without saying that this extraordinary percentage of success has not been maintained.

With regard to the causes of abortion one of our histologists has made an intensive study of all our suitable material, and found that about 85 per cent of the spontaneous abortions showed definite evidences of fetal or placental maldevelopment. Only about 15 per cent were due to apparent changes in the maternal organism of one sort or another. In studying the rare cases of true habitual abortion, however, there was a very low percentage of fetal abnormality and a slightly higher percentage of maternal abnormality. One might expect habitual abortion to be due to maternal disease or dysfunction unless, possibly, the woman is continuously producing defective ova.

As to the effectiveness of progesterone, I confess that on going over my first series, I found the results similar to those in the untreated series. Recently I learned from Dr. Falls that progestin extracted from the corpus luteum is much more effective than the synthetic product which we had been using.

When it comes to the general subject of abortion, not necessarily habitual abortion, there are many types of abortion due to fetal abnormality which cannot be corrected by progesterone. Neither would it influence the type of abortion due to such accidents as placenta previa or abruptio placentae, except in so far as it might lessen the irritability of the uterus to the extravasation of blood between uterine muscle fibers. It will be necessary to segregate as completely as possible the cases of abortion which are actually due to myometrial hyperirritability before a real evaluation of the efficiency of progesterone can be made.

DR. FRANK E. WHITACRE, NEW ORLEANS, LA.—The importance of the effect of coitus on abortion is not given its proper emphasis. Several years ago on our service in Peking, I appointed one of our staff women to question carefully these patients as to how many hours prior to the onset of a spontaneous abortion coitus had taken place. In a remarkable number, although exact figures are not available, there was a history that a few hours before spontaneous abortion coitus had occurred.

Coitus is mentioned in articles and textbooks, but not as one of the important causes. We know that abortion is more apt to take place at the time the patient would menstruate if not pregnant. The progesterone level may be affected at that time and there may be a hormonal response from the act which may raise the estrogen level, stimulating uterine contractions. Therefore, it is possible that many of these abortions are on a hormonal basis from coitus, rather than merely mechanical stimulation.

I was able to show recently the marked effect of psychic factors on the hormonal levels, under the title of "War Amenorrhea," in describing the effect of the bombings on women in Manila. I feel that the effect of coitus as a stimulant in spontaneous abortions is important.

DR. ARTHUR H. BILL, CLEVELAND, OHIO. In Dr. Quigley's paper and in the discussions which have followed, I have been surprised that so little was said about the retroverted uterus. This complication is tremendously overlooked and

even belittled by obstetricians who are treating these cases. In my experience, retroversion is one of the most common causes of miscarriage. I would never think it proper to leave a pregnant uterus in retroversion. The position should always be corrected and the uterus held in position by a retroversion pessary. As valuable as the form of treatment that has been described may be, I have personally seen many cases in which there have been repeated miscarriages in patients who have been treated by all these forms of therapy with no success while the presence of a retroverted uterus has been entirely overlooked. Patients of this kind may wear a pessary and go through a normal pregnancy without any medication.

Sometimes a patient may, on examination, be found to have a perfectly normal pelvic condition when she is not pregnant, but when she is six or seven weeks pregnant to have a retroversion. Furthermore, I would not take for granted that the patient will not have a retroverted uterus a week or two later just because it is normal on the first examination of pregnancy.

As valuable as this treatment is, and I believe that there is value in progesterone, one should not depend entirely on medication but should always correct a retroversion of the uterus.

DR. QUIGLEY (closing).—I did mention retroversion of the uterus in my paper and said that there should be care in looking after this condition, but perhaps did not emphasize it sufficiently.

Dr. Cooke's discussion was very interesting to me in regard to pathology of the ovum because it coincided with an opinion I have that this is less common in these cases of habitual abortion than we have thought.

I do not want to give the impression that I think giving progesterone is the only treatment for habitual abortion. All of my patients having a low metabolism rate were given thyroid. There is a function which progesterone performs aside from preventing uterine contractions, for it plays some part in nidation and has something to do with decidua formation.

DUPLICATION OF RIGHT KIDNEY PELVIS AND URETER WITH EXTRAVESICAL URETERAL OPENING*

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THE presence of an ectopic ureter presents a problem for the gynecologist since the great majority of cases producing symptoms are found in females. In 1936 Furniss collected and reported 240 cases of accessory ureters with extravesical opening. These included the cases collected and reported by Kilbane, Campbell, Thom, Sargent, and others. Lowsley and Conroy have estimated that there are approximately 300 such cases on record at the present time.

Ectopic ureters are found more frequently in females than in males, the ratio being about 2:1. The reason for this is that in the female an ectopic ureter usually opens distal to the vesical sphincter and produces a dribbling incontinence, while in the male it usually opens proximal to the vesical sphincter and is therefore asymptomatic. This dribbling incontinence in females is found present since birth, but in spite of this there is normal emptying of the bladder.

*Read at the Fifty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons, Hot Springs, Va., Sept. 7, 8, and 9, 1944.

According to Thom's series of 117 females with ectopic ureteral openings the locations were as follows: vestibule, 45; urethra, 37; vagina, 32; uterus, 3.

Embryology

Embryologically the secretory portion or cortex of the kidney is developed from an undifferentiated and unsegmented cell mass termed nephrogenic tissue. The ureter, renal pelvis, and collecting tubules, however, are formed by a separate "anlage" in the shape of a hollow bud arising from the mediodorsal aspect of the wolffian duct. In the 4.5 mm. embryo, the ureteral bud may be seen arising from the caudal end of the wolffian duct; it lengthens and grows cranially to enter the nephrogenic tissue forming a cap around its upper end which becomes flattened as the ureter lengthens and forms the major and minor calices and collecting tubules. As further growth takes place, the ureter and wolffian duct acquire separate openings into that portion of the cloaca which is destined to become the bladder.

The presence of an accessory ureter represents a regressive variation, and its ureteral bud arises from the wolffian duct usually a short distance cranial to the normal ureteral bud. As the wolffian duct orifice descends, the most caudally placed, or normal, ureter is the first to reach its position in the bladder. Because of a rotation and a growth of the tissue between this ureteral opening and the orifice of the wolffian duct, the upper ureter is carried caudalward so that it oftentimes becomes implanted at a point below the sphincter of the bladder.

Diagnosis

A dribbling incontinence of urine, in the presence of normal bladder function, is pathognomonic of ectopic ureter when occurring in a female. In the majority of instances this symptom has been present as long as the patient can remember. In a few reported instances incontinence is present only when the patient is in the upright position. Mulholland has reported a few cases of ectopic ureter in women where incontinence was not present. Judd reported the case of a 21-year-old girl who had diurnal incontinence during her entire life but had nocturnal incontinence only during the first few years. This led to an error in diagnosis so that the first operation performed for relaxed bladder sphincter was unsuccessful.

Much patience and diligence are often necessary in locating the orifice of the ectopic ureter. Attempts to locate the orifice of the ectopic ureter by means of intravenous injections of dyes are often unsuccessful because the fragment of kidney tissue drained by the accessory ureter may be so small or its function so impaired by infection that very little or no dye will be excreted. An intravenous pyclogram which shows multiple pelves on one side, and this in the presence of incontinence, should make one suspicious of an ectopic ureter. Crenshaw states that it is not absolutely necessary to demonstrate the orifice of the ectopic ureter if there is a history of dribbling and evidence of duplication of the renal pelvis by intravenous pyclography. Cystoscopic examination will usually demonstrate that the bladder and ureteral orifices are normal.

According to Weigert's law the ureter draining the upper part of the kidney opens lower in the urinary tract, and it is always this orifice

which is ectopic. Malgras asserts that this is not always true; however, the case to be reported here does conform to Weigert's law.

Treatment

The functional value of the kidney on the opposite side should be determined before any treatment is attempted. Heminephrectomy seems to be the procedure of choice where the segment of kidney drained by the ectopic ureter is small and therefore functionally of little value. Many cases have been reported in which there is a line of demarcation between the upper and lower kidneys. Ligation of the ectopic ureter below its pelvis with a separate ligation of the arteries and veins to the upper pole, followed by a "V" grooved incision through this line of demarcation, will produce a cure. Ligation of the ectopic ureter alone has not been as widely used but has some advocates. Implantation of the accessory ureter into the bladder may be of some value where the amount of kidney tissue involved is sufficient to be worth saving or where heminephrectomy is contraindicated. However, as Lowsley points out, the accessory kidney pelvis and ureter are usually infected, and therefore implantation may lead to an intractable cystitis.

Case Report

Miss A. S., 19 years of age, was referred by Dr. E. L. Tuohy on May 6, 1941, because of incontinence of urine. She had been working as a chambermaid in a hotel, and stated that she was in good health except for the present complaint. The family history and her past history were irrelevant.

Her chief complaint concerned a urinary incontinence, which on closer questioning was found to be a constant dribbling of urine both day and night, and had been present as long as she could remember. The patient's mother also stated that the incontinence had always been present. In spite of this the patient voided apparently normal amounts of urine at regular intervals. The urinary odor, due to the constant dribbling, was very annoying and made it difficult for her to keep a job and embarrassed her in her social contacts to such an extent that she was developing an inferiority complex. Two months previously the patient's tonsils had been removed as a possible cause for this continuous dribbling.

A general physical examination was negative except for the pelvic condition, which, on examination of the vagina, revealed a relaxation of the anterior vaginal wall on the right side. On palpation, this mass felt like a dilated urethra in that it was soft and not tender. The bimanual and rectal examinations were otherwise negative. The blood counts were as follows: hemoglobin, 81 per cent; red cells, 4,180,000; white cells, 10,500. The catheterized urine specimen was negative. The blood pressure was 112/70. The Kline exclusion test was negative. Methylene blue was instilled into the bladder, and it was felt that there was very little sphincter resistance when the catheter was passed. The vagina and vulva were then packed with cotton in an attempt to locate an anomalous opening from the bladder but after a period of one hour no dye had appeared on the cotton, but a portion of the cotton was moist and had an odor of urine. Roentgenographic plates of the spine failed to reveal any evidence of spina bifida.

The following day a cystoscopic examination was performed by Dr. W. E. Hatch, and the bladder and ureteral orifices appeared to be normal. Cystograms were also made but failed to reveal any evidence of a diverticulum or other abnormality. Because of the constant dribbling of urine, it was felt that there must be an anomalous opening of some sort, so methylene blue was again instilled into the bladder and, with

the patient in the lithotomy position, the vulva and perineum were observed constantly for a period of an hour and fifteen minutes when suddenly a small bead of fluid appeared to come out of a slit in the mucosa at a point which was approximately $1\frac{1}{2}$ cm. below and to the right of the urethral orifice. A probe could be introduced into this slit for a distance of 4 centimeters. With the aid of a blunt-tipped needle a solution of skiodan was then injected into this orifice, and a filling was obtained which extended up through a very tortuous and dilated ureter into a small sacklike pelvis which was located on the upper part of the right kidney.

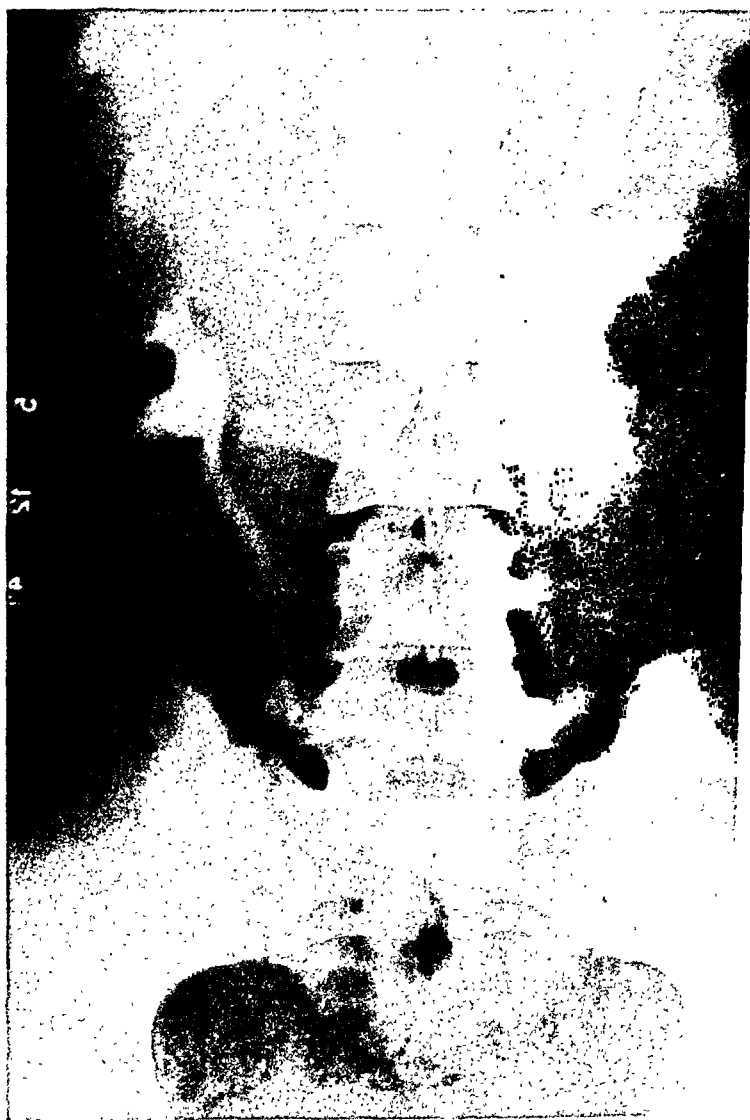


Fig. 1.—Bilateral excretory pyelogram showing duplication of the right kidney pelvis.

An intravenous pyelogram was then made to determine the presence of a functioning kidney on the opposite side. This pyelogram showed a duplication of the right kidney pelvis and ureter and a normal appearing kidney pelvis and ureter on the opposite side (Fig. 1). Retrograde pyelograms were then made with a filling of the normal ureter on the right side and also of the ectopic ureter so that both could be shown on the same plate. This showed the double kidney pelvis on the right side with double ureters, the ureter from the upper pelvis having its opening in the vestibule (Fig. 2).

Surgical treatment in the form of a heminephrectomy was advised and the patient consented. On June 3, 1941, under ethylene-ether-anesthesia, a right curved loin incision was made to expose the right kidney. The superior pole was easily delivered bringing into view the small sacklike pelvis and dilated ureter. After isolation and ligation of

the blood supply to the upper part of the kidney and the ureter to the upper pelvis, a "V" grooved incision was made through an isthmus which seemed to separate the upper and lower kidneys, and the upper portion was removed. Mattress sutures were inserted to close the "V" incision, and pieces of fat tissue were interposed before the mattress sutures were tied. Urine continued to dribble from the ectopic ureter for a period of forty-eight hours following the operation, apparently due to the accumulation of urine in the dilated ureter. However, the patient made an uneventful recovery and was discharged from the hospital on the tenth postoperative day.

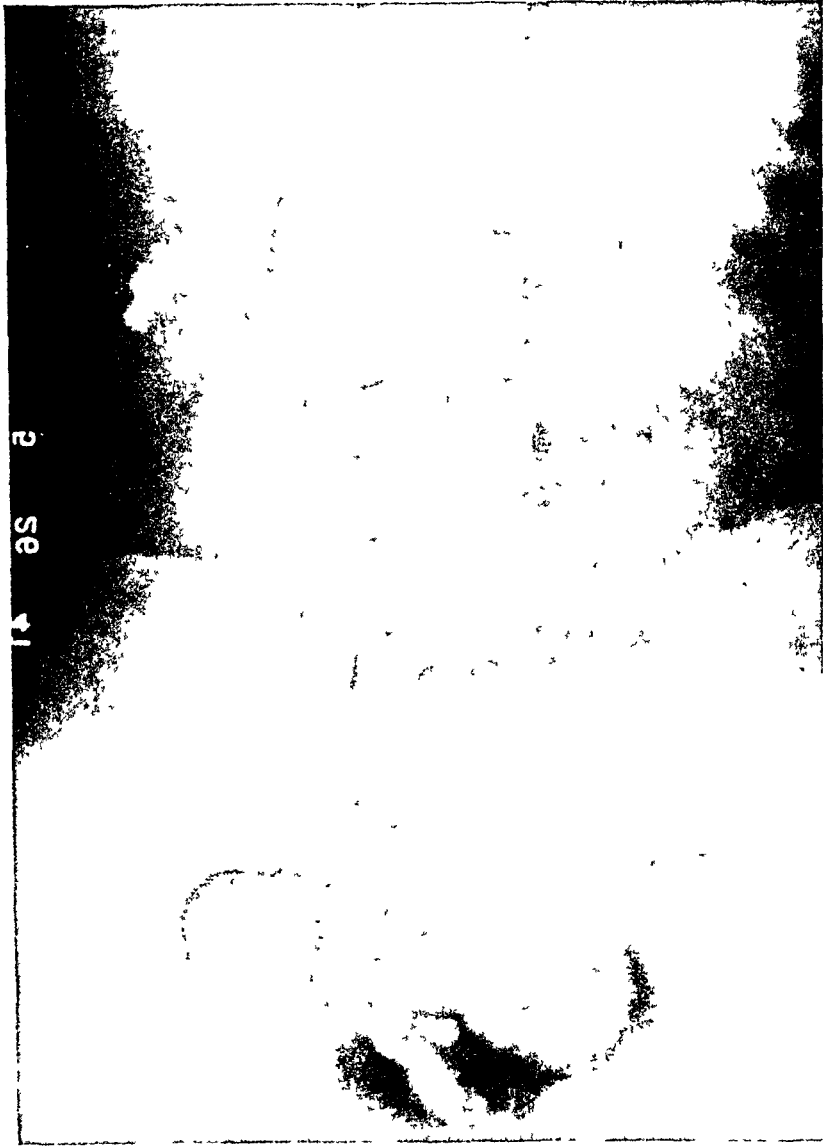


Fig. 2.—Retrograde pyelogram showing normal lower kidney pelvis and ureter and small saclike upper kidney pelvis with greatly dilated ureter.

Examination of the surgical specimen revealed a small saclike pelvis and an amount of kidney tissue equal to approximately one-fifth of the remaining kidney tissue on the right side. The blood supply consisted of one artery and one vein. There was chronic inflammation of the accessory pelvis and ureter. The submucosa of the pelvis and ureter was thickened, edematous, and infiltrated with a moderate number of scattered lymphocytes. The interstitial connective tissue of the muscular layers of the wall of the pelvis was also infiltrated with a few scattered lymphocytes.

The patient was last seen approximately two years after the heminephrectomy was performed. There were no complaints and it was apparent at that time that the inferiority complex had completely disappeared. She had become a social as well as economic asset to the family.

Conclusions

1. Constant dribbling of urine in the presence of normal bladder function should suggest the presence of an accessory ureter with an extravesical opening.
2. Intravenous urography is a valuable procedure in establishing the diagnosis of this anomaly.
3. The location of the orifice of the ectopic ureter is often difficult.
4. Heminephrectomy is the procedure of choice.

References

1. Campbell, M. F.: Ectopic Ureteral Orifice; 17 Cases in Children, *Surg., Gynec. & Obst.* 64: 22, 1937.
2. Crenshaw, J. L.: Ureter With Extravesical Orifice, *J. Urol.* 43: 82, 1940.
3. Crenshaw, J. L., and Buchtel, H. A.: Ectopic Ureter With Extravesical Orifice, *J. Urol.* 35: 190, 1936.
4. Furniss, H. D.: Supernumerary Ureters With Extravesical Openings, *J. Urol.* 37: 341, 1937.
5. Judd, E. S.: Supernumerary and Single Ureters Opening Extravesically, *Surg., Gynec. & Obst.* 27: 13, 1918.
6. Kilbane, E. F.: Ectopic Ureteral Openings; Surgical Significance and Treatment, *Surg., Gynec. & Obst.* 42: 32, 1926.
7. Lowsley, O. S., and Conroy, F.: Aberrant Ureter and Its Treatment, *J. Urol.* 48: 611, 1942.
8. Malgras, P.: Extravesical Openings in Females, *J. d'urol.* 42: 269, 1936.
9. Meyer, R.: Personal communication.
10. Mulholland, L. W.: Duplication of Ureter With Extravesical Opening, *J. Urol.* 41: 220, 1939.
11. Priestley, J. T., and Schulhof, M. G.: Heminephrectomy for Duplicated Kidney and Ectopic Ureter, *Proc. Staff Meet., Mayo Clin.* 12: 622, 1937.
12. Sargent, J. C.: Ureteral Ectopia, *J. Urol.* 23: 357, 1930.
13. Thom, B.: Surgical Treatment of Double Ureters and Double Kidneys and of Ureters Opening Extravesically, *Ztschr. f. Urol.* 22: 417, 1928.

Discussion

DR. WILLIAM A. COVENTRY, DULUTH, MINN.—This paper shows the value of patience when one must observe for over an hour to find evidence of a moist spot from an aberrant ureter. I would expect more excoriation of the vulva from such a leak, but apparently the amount of urine excreted was so small that there was total absorption by the vulva pads worn.

One might discuss whether implantation of an aberrant ureter in the bladder would be worth while, a procedure advocated by some operators. The question of tying of the ureter alone may also be raised. It seems to me the procedure carried out by Dr. Moe is probably the best, because if the ureter is infected, one is sure to have an infected bladder.

The value of proving the presence and function of the opposite kidney is apparent, especially when it is likely that if one anomaly is present, one might expect another anomaly. The tortuosity of the abnormal ureter is interesting and offers an opportunity for speculation as to its cause.

DR. B. Z. CASHMAN, PITTSBURGH, PA.—In 1928 I reported to this Association an almost identical case as that reported by Dr. Moe. My patient was 16 years of age and had a small amount of urine dribbling almost constantly as long as she could remember. The amount was not large and it was the urinous odor that annoyed her more than anything else.*

DR. MOE (closing).—Dr. Cashman calls attention in his case to a point which is very valuable, namely, the insertion of a catheter into the normal ureter on the same side as the ectopic ureter. That is of great help according to the reports in the literature, when at operation one cannot decide which ureter he is dealing with. If one is excising the accessory kidney it is not so difficult, but the men who have advocated merely ligation of the ureters have stressed the point that a catheter should be placed in the normal ureter at the time of operation.

(Conclusion of Transactions of the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons)

*See Tr. Am. A. Obst. & Gynec. 41: 329, 1928.

Original Communications

POSTMENOPAUSAL PRURITUS VULVAE*

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PRURITUS vulvae in the postmenopausal woman poses a clinical problem of the greatest magnitude. It is frequently encountered, is extremely discomforting to the patient and according to most reports, is seldom handled successfully. The problem is so ubiquitous and formidable that dermatologists, gynecologists and endocrinologists often refer these cases to each other. Everyone seems anxious to place this complaint in the other specialist's field.

Postmenopausal pruritus vulvae differs from the pruritus vulvae of the less mature woman in several respects, the most important being the relative infrequency of specific infections and the introduction of the atrophy process in the external genitalia. It is recommended that after pediculosis pubis, diabetes mellitus and specific local skin diseases have been excluded, that the physician approach the problem with this medical philosophy, namely, that any area of skin can be responsible for the sensation of itching if the proper combination of skin irritation and receptiveness to that irritation is present. The percentage values of the irritation and the skin's receptivity to it may vary within the combination, but the total of the two must attain a certain threshold height for the pruritic sensation to be aroused.

It becomes apparent here, that the examiner must have sufficient knowledge of gynecologic techniques to evaluate the presence and the source of any irritating discharges. Rectal discharges are seldom of importance here. They are chiefly responsible for pruritus ani. Of more interest is the possibility of urinary incontinence. A normally alert woman is seldom unaware that she is not controlling her urine properly. Usually, she is cognizant of even minute urinary incontinence, but she may not relate it to her pruritus. It is the examiner's duty to question these old women about this possibility because incessant wettings of the labia by urine is a cause of pruritus vulvae, and it can be well controlled by pessaries or proper plastic vaginal surgery.

Vaginal discharges are the chief causes of vulvar irritation. The distribution of the itching areas will often call the examiner's attention to the possibility of a vaginal discharge, although the vulva may be quite clean at that time. If the areas involved are confined to the lower halves of the labia minora and majora and to the perineum, leaving the clitoris area relatively free, one must thoroughly explore the possibility of an irritating vaginal flow. This impression may be re-enforced by information from the patient that the itching is more intense during the day than at night. Obviously, vaginal secretions will be forced out of the

*Read at a Symposium on Clinical Problems Associated with Aging, at the Annual Meeting of the American Geriatrics Society, on June 10, 1944, in New York City.

vagina and on to the perineum and labia to a greater extent when the patient is active. At night, when she is relatively inactive, less of the irritating vaginal secretion will come in contact with the external genitalia.

The principal types of vaginitis which are responsible for pruritus vulvae are the *Trichomonas vaginalis*, Monilia and senile ones. The first two varieties are only seldom encountered in postmenopausal women. They are easily identified by the trained observer, and positive laboratory identification is a simple matter. The therapy of both these conditions has become standardized and is satisfactory although often prolonged and tedious.¹⁻²

Senile vaginitis, although it is the type of vaginitis most often encountered in postmenopausal women, is not as frequent an etiologic factor of pruritus vulvae as the current literature would have us believe. One seldom sees a case of senile vaginitis in these women which is severe enough to produce a vaginal discharge sufficiently profuse to flow out of the vagina in any appreciable quantity.



Fig. 1.—A 65-year-old woman who never complained of pruritus vulvae. The epidermis is normal. The derma is free from any sign of inflammation.

The appearance of the vagina makes the diagnosis. Corroboration is secured if a smear of the vaginal secretion reveals a Grade I cytology. Here, there is little evidence of cornification of any of the epithelial cells, a moderate number of cells from the basal layers of the epithelium is present and an abundance of leucocytes “dirty” the smear.³

This type of vaginitis yields readily to ordinary astringent tamponades and cleansing douches. Relief is obtained faster if estrogenic vaginal suppositories are employed at night before retiring. The use of estrogens by the oral and parenteral routes is not recommended. Most of these women have become accustomed to getting along on a very low systemic level of estrogens. Their estrogenic titers in the urine and blood are small.⁴ It is inadvisable to again subject their entire organism to the multiple effects of systemic estrogenic medication. Many of these older women develop annoying symptoms under these circumstances.

We prefer to use estrogens incorporated in vaginal suppositories which allow the hormones to be applied locally where their effect is most required.⁵ Thus, they are effective in concentrations which are far too low for generalized effects.

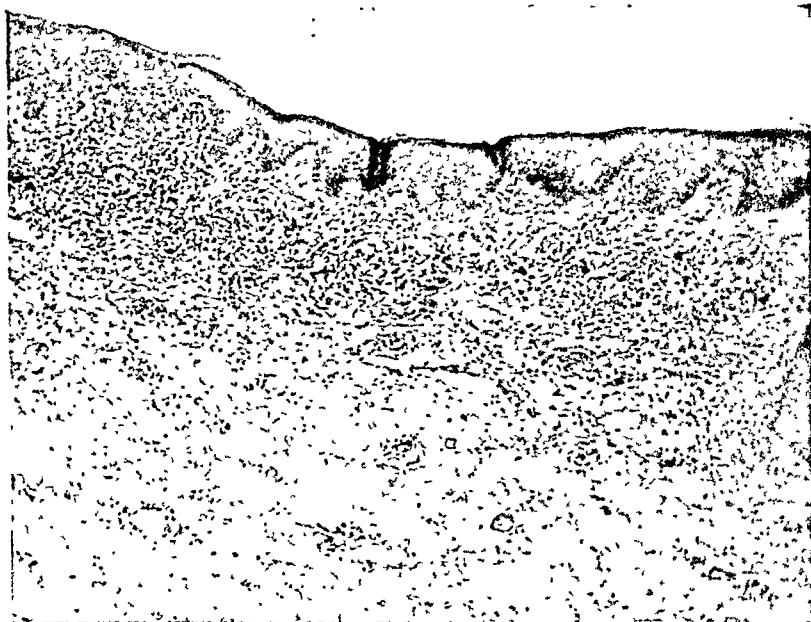


Fig. 2.—A 45-year-old woman, complaining of pruritus vulvae; macroscopically, a case of simple atrophy. Note the thin but normal epidermis. The derma exhibits a broad zone of inflammation, which extends into the papillae.

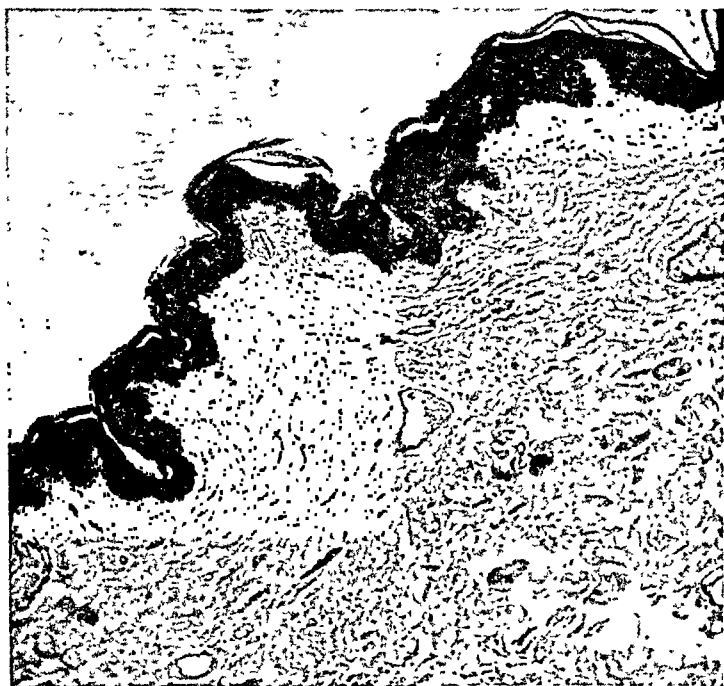


Fig. 3.—Posttherapy section after a clinical cure. The derma now shows no signs of infection.

Up to this point, we have limited our discussions to the principal vulvar irritants. However, there are a host of minor offenders, some constantly present, which assume considerable stature if the resistance of the vulvar skin declines and its receptivity to noxious stimuli increases. Among these irritants are pathogenic skin organisms, the minimal discharge from a normal vagina, an occasional few drops of urine, sweat and friction from clothes and cleansing paper. These irritants as already stated assume importance only when the resistance of the skin to infection and irritation declines.

It has been our experience to find the majority of our cases of pruritus vulvae in women past the menopause to be due to changes in the vulvar skin rather than to unusual irritating substances. It is only logical to assume that the aging process will bring about profound changes in the external genitalia, and this we have found to be true.

It is my opinion that we may recognize three types of vulval pathology in pruritus: Atrophy, lichenification and leucoplakia. These lesions have distinctive macroscopic and histopathologic characteristics, which are more or less constantly recognizable. I am unwilling to accept the traditional term "kraurosis vulvae" as a designation of a disease entity. I do not believe that a sufficiently characteristic macroscopic or microscopic picture exists to justify the use of kraurosis vulvae as an entity.

If one compares the macroscopic and microscopic descriptions which the acknowledged authorities on the subject have assigned to this condition, the most varying pictures are portrayed, and only utter confusion results. Etymologically, kraurosis means shrinking, and if the traditionalists insist on the use of the term, I recommend it to be limited to the description of accentuations of the normal vulval atrophy processes.⁶

We are unable to subscribe to the use of a single term to encompass all the conditions met with in pruritus vulvae. Chronic atrophic vulvitis, leucoplakic vulvitis and leucokraurosis are all inadequate in some respects and misleading in others.

Bonney⁷ distinguishes four stages of the disease of leucoplakia. Taussig⁸ believes that there are three stages in leucoplakic vulvitis. Adair and Davis⁹ distinguish several stages as does Montgomery.¹⁰ I should like to point out here that in order to distinguish authoritatively the stages of any pathologic process, one must obtain a series of biopsies from a given lesion in an untreated patient.

I know of no one so scientifically detached as to permit a case of postmenopausal pruritus vulvae to go untreated, while he obtained a series of biopsies. To the best of my knowledge, the histopathologic specimens have been obtained from the untreated patient only once, from patients who have had vulvectomies, from the vulvectomy specimen itself and from cadavers.

The authenticity of the description of the stages of leucoplakia of the vulva and so-called kraurosis of the vulva, or the combination of the two, may well be questioned.

In addition, I should like to point out that vulvae which macroscopically present absolutely typical conditions, often yield biopsies which are quite varied. When these slides are presented without accompanying histories to competent dermatologists, they are often unable to make the correct diagnosis which their unaided eyes would have recognized immediately. A prominent dermatologist has often assured me that, barring malignancies, if he is unable to diagnose a skin lesion by inspection and palpation, the microscope will be of little further aid to him!¹¹

It is my belief that there is a simple explanation of these conflicting facts. There are common etiological factors in most cases of postmenopausal pruritus vulvae, and the response of the skin to these factors varies with the individual. The varied macroscopic and micro-

scopic pictures one encounters in these cases are merely the resultants of the patient's capacity and manner of response to the same set of stimuli. They are not different disease processes.



Fig. 4.—A 58-year-old woman with pruritus vulvae, and a macroscopic picture of lichenification of the vulval skin. The epidermis is only moderately thickened. The pars papillaris of the derma shows an inflammatory reaction.



Fig. 5.—Posttherapy section after a clinical cure. There is some evidence of hyperkeratosis in this field. The derma is now free from infection.

As we have already pointed out, the etiological factors in these cases are always present. They are the relatively nonpathogenic skin organisms, the irritations of friction and the various discharges to which the vulva is subject. These factors become potent only when the normal processes of atrophy permit them to penetrate the weakened skin, set up a localized zone of inflammation and cause pruritus. The itching then adds the trauma of scratching to the list of offenders and the sub-epithelial infection becomes chronic. In the necessarily slow healing process which follows, we have the explanation of the lichenification and the keratosis which are the characteristic features of pruritus vulvae. This, in a nutshell, is the probable explanation of all vulval pruritus, postmenopausal.

While vulval pathology in pruritus may be divided into three types—atrophy, lichenification or lichenization and leucoplakia—a fourth type of disease, lichen sclerosus and atrophicus is sometimes encountered, but it does not merit a detailed discussion.¹²

In atrophy of the vulva, the skin eventually acquires a yellowish tinge, although in the early stages of the process, it is often dark red or purple. It seems transparent and feels thin. The hair is brittle and scanty and the term “parchment paper” may well be applied. The labia majora and minora are considerably reduced in size, and in extreme cases, practically disappear. The vaginal orifice is often narrowed to the point where only one finger can be inserted.

Microscopically, very few changes can be observed. The epithelium is usually quite thin. Stains for fat reveal the almost total absence of this material from the dermis, but elastic tissue stains show no changes from the normal.

Lichenification of the vulva presents the same picture other portions of the cutis do when they are involved in this process. The integument is thickened and becomes a mosaic of small flattened elevations, separated from each other by distinct depressions. The color varies from yellowish brown to dusky red. Occasionally, the skin has a soggy, white appearance.

The histopathologic findings are hyperkeratosis, spongiosis and acanthosis. The subepithelial tissue is edematous, and is infiltrated by lymphocytes and plasma cells.

Leucoplakia of the vulva is easily distinguished macroscopically. It presents the same appearance as leucoplakia of the mouth. It is present on the vulva as a series of slightly elevated plaques or striae, gray to blue-grayish in color. The skin or mucous membrane may be involved, and when affected, they both are thickened.

The histologic picture of the disease is much disputed.^{7-8, 12-13} As we have already stated, it is our contention that the histopathologic findings vary with the individual's response to the stimulus of relative vulval irritation. The different descriptions of the histopathologic processes may well be explained by this fact.

The epidermis in leucoplakia always shows some acanthosis and hyperkeratosis. Parakeratosis may occasionally be demonstrated. The evidence of a dyskeratotic process is quite constant. The changes in the corium are most varied, but signs of an inflammatory process are always present. There is an infiltration of lymphocytes, polymorphs and plasma cells in the pars papillaris of the derma. I have never been able to demonstrate distinctive changes in the elastic fibers. Any liquification necrosis that may be present seems confined to the basal-cell layer of the epidermis.

My aims in the therapy of postmenopausal pruritus vulvae are well expressed by the Latin tag *noli me tangere*. Avoid irritating an already irritated and infected skin. This is accomplished by directing the patient to keep the affected area constantly covered with a thick coating of bland ointment. A base of petrolatum alba with 20 per cent starch and thirty per cent zinc oxide is an ideal preparation. This crême is kept on the vulva for the minimum of three weeks, and the patient may cover it with squares of gauze to protect her clothing. As the

salve wears off, more is added. The patient may bathe as often as she desires, but she is not to attempt to clean off the salve. After her bath, she replaces the ointment washed away.

It is inadvisable to incorporate antipruritics in the salve. While they may afford temporary relief, they soon become ineffective, and all of them are irritants to some degree. In my experience, oil of cade, phenol, menthol, resorcin, calmine and the coal tar products eventually aggravate the pruritus.



Fig. 6.—A 62-year-old woman with pruritus vulvae. Macroscopically, a typical case of leucoplakia. There is evidence of hyperkeratosis and acanthosis. A broad zone of inflammation runs through the entire derma.



Fig. 7.—Posttherapy section after a complete clinical cure. There is still evidence of dyskeratosis. There is no longer a continuous zone of inflammation in the derma. There are focal areas of increased cellular density. High power examination reveals the cellular elements to be connective tissue. There are no neutrophils and only an occasional lymphocyte.

The constant application of the bland ointment protects the vulval tissues from all irritants and gives them the opportunity of coping with the dermal infection. Scratching is reduced considerably, since it is now mechanically unsatisfactory. After three weeks, as the pruritus abates, one may restrict the use of the ointment to nights only. The *crème* may be removed in the daytime, but the cleansing process must be accomplished by the use of cottonseed oil, mineral oil or salad oil. Soap and water may not be used for this purpose since this combination is irritating and requires too much rubbing.

In addition to this simple method of protecting the skin from infection and irritation, one must direct attention toward combating the extreme effects of atrophy of the external genitalia. In other words, we should attempt to increase the resistance of the skin besides protecting it from harm.

I recommend the use of large doses of vitamin A in the form of concentrated fish oils. The experimental skin lesions resulting from deficient vitamin A diets exhibit a type of hyperkeratosis and dyskeratosis which is similar to that found in pruritus vulvae.¹⁴ One must recall that vitamin A has been demonstrated to possess the ability of increasing the body's resistance to infections. It is not my intention to proclaim vitamin A the "anti-infection" vitamin, but one cannot ignore its proved infection-resisting quality.¹⁵

In questioning these older women who suffer from pruritus vulvae, I have often noted how restricted is their diet. Many of them avoid the majority of the vitamin A rich foods. Furthermore, the absorption of vitamin A and carotene from the intestinal tract is dependent upon normal fat metabolism. Liver cirrhosis will further prevent the conversion of carotene into vitamin A and will interfere with body storage.¹⁶

While it is true that only a few milligrams of vitamin A are required to satisfy man's minimal daily requirements, the combination of restricted diets and poor absorption can be responsible for an avitaminosis.

Attempts have been made to combat pruritus vulvae with estrogenic ointments.¹⁷ It is our experience that these preparations are unavailing in the treatment of postmenopausal pruritus vulvae. It has never been demonstrated that the estrogens have any effect on human skin, although we are all familiar with the responses of the vaginal mucous membrane to these hormones.

Estrogens used locally or systemically will cure senile vaginitis, but as we have already pointed out, senile vaginitis is rarely the cause of postmenopausal pruritus. In these older women, vaginal inflammations seldom develop a discharge profuse enough to flow out of the vagina and irritate the vulva.

It is claimed that estrogens will aid in combating atrophy of the external genitalia. This fact has not been substantiated by clinical results. One could scarcely expect the external genitalia to react to estrogenic therapy since the tissues usually are no longer capable of responding in a normal manner to the intrinsic ovarian steroids of the patient. A considerable percentage of postmenopausal women have a high estrogen level as can be proved by urine assays.¹⁸ Furthermore, cases of pruritus vulvae which exhibit atrophic and leucoplakic changes have been ob-

served in younger women who are menstruating regularly. Presumably their gonads are functioning normally, but the vulva has lost its ability to respond to the ovarian hormones.

Androgens, on the other hand, have proved effects on skin. Testosterone propionate stimulates the sebaceous glands and causes oiliness of the skin and hair. This hormone induces the sebaceous glands to secrete a soft, white, odoriferous material, and it has been reported that the vulval skin of castrated women participates in this secretory activity.¹⁰

It has also been demonstrated that androgens increase skin vascularization. Testosterone propionate dilates skin blood vessels, increases the blood's content of oxyhemoglobin, and stimulates the rate of blood flow.²⁰⁻²¹

With these skin reactions to the androgens in mind, we have used an androgenic ointment instead of our usual bland ointment in the treatment of those cases of pruritus vulvae where the outstanding macroscopic and histopathologic feature was atrophy. Observers familiar with the dry, thin, transparent skin of many of these cases, can readily appreciate the rationale of using a hormone which promises to stimulate the secretion of sebum and to increase skin vascularization.

In my hands, androgenic ointments have been successful in relieving pruritus vulvae. It is my impression that results are obtained more quickly with androgenic ointments than with the simple bland ointment in those cases which exhibit extreme grades of atrophy. However, I am not as yet prepared to state that my posttherapy biopsy material shows a qualitatively different picture after the use of the bland and the androgenic ointments. This picture, in cases which have been relieved of their pruritus, demonstrates the disappearance of the subepithelial inflammatory process. This infection by its very location must irritate the nerve terminations in the papillae of the derma, and in my opinion, it is the cause of all postmenopausal vulval pruritus.

Every biopsy we ever obtained from the vulval region of postmenopausal women complaining of pruritus vulvae clearly demonstrated an inflammatory process in the derma. All of our cases in which we obtained relief from the itching and were able to obtain posttherapy biopsy specimens showed a complete or almost complete disappearance of this infection. These findings were consistent regardless of the therapeutic regimen we employed.

I have been using a preparation containing 2 mg. of testosterone propionate to the gram of ointment.* It is employed exactly like the bland ointment. Since this hormone crème is expensive, it should be employed only where vulval atrophy is pronounced.

I believe that the use of the roentgen ray is not indicated in the treatment of postmenopausal pruritus vulvae. Clinical results are poor. Occasionally, temporary relief is obtained, but this is by no means the usual occurrence. In practically all instances, the pruritus is ultimately aggravated, probably because the atrophy of the genitalia is intensified by the action of the rays.

In my hands, the local injection of alcohol, as advocated by Wilson,²² has not been satisfactory. I have also injected histamine²³ and a com-

*Perandren Ointment supplied through the courtesy of Emile S. Fromer of the Ciba Pharmaceutical Products, Inc., Summit, N. J.

bination of procaine and benzyl alcohol in oil²⁴ without obtaining relief from itching. I have no experience with tattooing of the vulval skin,²⁵ but it seems to me that all these injection plans merely add insult to the already injured skin.

I have been able to secure pretherapy and posttherapy vulvar biopsies from fourteen cases of postmenopausal pruritus vulvae. The biopsies were all obtained from the inner surface of the left labia majora in the region of the clitoris, using local procaine anesthesia.

Although we have treated almost one hundred cases of postmenopausal pruritus vulvae during the past six years, we regard only these fourteen as complete studies. If biopsies are not obtained before and after the completion of therapy, it is not possible to truly evaluate the efficacy of any scheme of therapy. The subjective responses of the patient are a barrier to scientific clarity. Only too often have I suspected some of my older clinic patients of giving the investigator the answer they thought he wanted to obtain.

All of our fourteen cases were free of excessive vaginal discharge. None of them had diabetes, local parasites or specific skin diseases. All of them had the severest type of subjective symptoms. Every one had had previous therapy which ran the gamut from local applications and injections to parenteral hormonal therapy and x-ray exposures. The shortest period of observation since the final biopsy is now three months. The longest period is four years. Five cases of leucoplakia are included in this series.

We obtained satisfactory clinical results in all of these cases. The results ranged from perfect cures to cases where occasional recourse to ointment therapy as outlined here is necessary. I should like to be the first to point out that it is scarcely possible that any woman suffering from this complaint would submit to a posttherapy biopsy unless she had received satisfactory relief from her pruritus. This is the probable explanation of the almost perfect results recorded in those patients, who submitted to more than one vulval biopsy.

The posttherapy biopsies all show a marked diminution or complete disappearance of the inflammatory process in the pars papillaris of the derma. In the leucoplakic cases, dyskeratosis of the epithelium was still evident, but there no longer was any evidence of infection in the corium.

Summary

The theory is advanced that most cases of postmenopausal pruritus vulvae are basically due to a local atrophy of the skin. This permits an invasion and infection of the derma by the usual pathogenic skin organisms, which are always present in that region. The resulting inflammation affects the nerve terminations in the papillae of the derma and produces the itching. The macroscopic and microscopic pictures are largely determined by the individual's defense reactions. The same stimulus which will result in lichinification in one person will cause leucoplakia in another.

I believe that the best method of obtaining relief is to protect the skin from further irritation by the constant application of a bland ointment for at least three months.

An androgenic ointment should be used locally in those cases which exhibit severe vulval atrophy.

The successful treatment of fourteen cases of severe postmenopausal pruritus vulvae in which pretherapy and posttherapy vulval biopsies were obtained are reported. Five of these patients had leucoplakia of the vulva.

References

1. Novak, E.: *Gynecology and Female Endocrinology*, Boston, 1941, Little, Brown & Co., p. 153.
2. Novak, E.: *Gynecology and Female Endocrinology*, Boston, 1941, Little, Brown & Co., p. 156.
3. Papanicolaou, G. N., and Shorr, E.: *AM. J. OBST. & GYNEC.* 31: 806, 1936.
4. Fried, S. Chas.: *Glandular Physiology and Therapy*, Chicago, 1942, American Medical Association, p. 350.
5. Neugarten, L., and Steinitz, E.: *J. Clin. Endocrinol.* 1: 754, 1941.
6. Breisky, A.: *Zeitschr. f. Heilk.* 6: 69, 1885.
7. Bonney, V.: *Lancet* 1: 1465, 1908.
8. Taussig, F. J.: *Diseases of the Vulva*, New York, 1931, D. Appleton & Co., p. 149.
9. Adair, F. L., and Davis, M. E.: *Surg., Gynec. & Obst.* 61: 443, 1935.
10. Montgomery, H.: *Arch. Dermat. & Syph.* 30: 80, 1934.
11. Lapowski, Boleslaw: Personal communication.
12. Hunt, E.: *Diseases Affecting the Vulva*, London, 1943, H. Kimpton, p. 84.
13. Graves, W. P.: *Gynecology*, Philadelphia, 1928, W. B. Saunders Co., p. 264.
14. Schultz, F. W.: *Mississippi Doctor* 19: 279, 1941.
15. MacKay, H. M.: *Arch. Dis. Child.* 9: 133, 1934.
16. McDonald, P. R.: *Pennsylvania M. J.* 44: 699, 1941.
17. Mishell, D. R., and Motylloff, L.: *AM. J. OBST. & GYNEC.* 39: 796, 1940.
18. Cinberg, B. L.: *A Manual of Endocrine Therapy*, New York, 1942, Chemical Publishing Co., p. 17.
19. Hamilton, J. B.: *J. Clin. Endocrinol.* 1: 567, 1941.
20. Hamilton, J. B.: *Endocrinology* 21: 649, 1937.
21. Edwards, E., et al.: *Endocrinology* 28: 119, 1941.
22. Wilson, W. M.: *J. A. M. A.* 110: 493, 1938.
23. Lavandhomme, Bruxelles méd. 19: 1330, 1939.
24. Reich, W. J., Button, H., and Nechtow, M. J.: *AM. J. OBST. & GYNEC.* 45: 1036, 1943.
25. Turell, R.: *AM. J. OBST. & GYNEC.* 42: 290, 1941.

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PENICILLIN TREATMENT OF SULFONAMIDE-RESISTANT GONOCOCCAL INFECTIONS IN THE FEMALE*

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THE use of penicillin therapy in the control of gonococcal infections in the female has already been reported by several investigators.¹

A preliminary report on the successful penicillin treatment of sulfonamide-resistant gonococcal infections in 44 female patients under our care appeared in the *Journal of the American Medical Association* of April 8, 1944.² The present paper deals with the analysis of the ad-

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ditional results obtained in 108 hospitalized female patients suffering from gonococcal infections, who were treated with varying amounts of penicillin.

Clinical Material

A total of 108 adult female patients was diagnosed as *gonococcus* positive by cultures and/or smears during a 9-month period, from September, 1943, to June, 1944.

The urethra alone was found to be infected in 3 cases; the cervix alone in 39. A concurrent urethral and cervical infection was present in 66 women. Adnexal involvement was observed in 34 patients, although it was of a severe character only in exceptional cases. This paucity of acute adnexal disease may have been due to the long duration of the infection which averaged 70 days, and to the fact that the majority of the patients had already received two or more courses of sulfonamide in addition to other supportive therapy. One patient suffered from a diffuse peritonitis. Another developed arthritis of the right elbow during the course of penicillin treatment. Pregnancy ranging from 3 to 9 months was present in 6 patients.

Prior to penicillin treatment, 101 of these patients had failed to respond to at least two courses of 20 Gm. each of various chemotherapeutic agents of the sulfonamide group. The remaining 7 patients received penicillin treatment because they had shown a marked sensitivity to the sulfonamides.

Schedule of Treatment and Dosage

In order to determine a simple yet adequate schedule of penicillin treatment for sulfonamide-resistant gonococcal infections, the following plan was adopted: Two constant factors were maintained throughout the study: (1) A 3-hour interval between successive injections of penicillin, and (2) The intramuscular injection in the gluteal region.

The variable factors were: (1) the administration of varying amounts of penicillin, i.e., from 25,000 to 100,000 Oxford Units, as total dosage, and (2) the variation of the total period of time during which the total amount of penicillin was administered.

Three different brands of penicillin were investigated: Reichel Laboratories, Pennsylvania; E. R. Squibb & Sons, New York; Charles Pfizer, New York, but no essential differences of reactions or efficacy were observed. Each 5,000 Oxford Units of penicillin was dissolved in 1 c.c. of sterile normal saline.

The following table shows the number of hospitalized patients treated, the time required for each treatment, the amounts of single doses and the total dosages of penicillin, and finally the therapeutic results obtained.

Results of Therapy

All 108 patients treated with penicillin became bacteriologically negative with regard to cervical and urethral cultures. As may be seen in Table I, 99 patients who received varying amounts of penicillin over different periods of time, responded to a single course of therapy. The remaining 9 patients, who did not respond to the initial treatment, were cured by a second course of 100,000 O.U. given in divided doses of 25,000 O.U. each at 3-hour intervals.

TABLE I

SCHEDULE NO.	NO. OF PATIENTS TREATED	NO. OF INTRA-MUSCULAR INJECTIONS	HOURS RE-QUIRED FOR TREATMENT	OX-FORD UNITS PER DOSE	TOTAL DOSAGE OF PENICILLIN O. U.	NO. OF PATIENTS	
						CURES	FAILURES
I	12	5	12	20,000	100,000	12	—
II	11	4	9	25,000	100,000	11	—
III	21	3	6	25,000	75,000	20	1
IV	15	2	3	25,000	50,000	12	3
V	29	2	3	50,000	100,000	28	1
VI	10	1	6	50,000	100,000	10	—
		2		25,000			
VII	1	1	3	50,000	75,000	1	—
		1		25,000			
VIII	1	3	6	20,000	60,000	1	—
IX	4	1	—	25,000	25,000	2	2
X	2	1	—	50,000	50,000	1	1
XI	2	1	—	75,000	75,000	1	1

Following penicillin treatment daily clinical and bacteriologic examinations of the hospitalized patients were performed. The patients were followed up for an average period of 7.8 days, during which an average of 5.7 examinations were carried out.

Reversal from positive to negative of the initial bacteriologic findings took place within 24 hours after termination of penicillin therapy in all but one case. In the one exception, reversal occurred after 48 hours. Among seven cases in which cultures were taken at hourly intervals after treatment had been initiated, three became negative within 2 hours.

The following factors seem to determine the therapeutic efficacy of penicillin in the treatment of sulfonamide-resistant gonococcal infections. (1) The administration of an optimal amount of penicillin: In this study, this amount proved to be a total dosage of 100,000 O.U. (2) The total period of time during which the total amount of penicillin was administered: 6, 9 and 12 hours were all found to be satisfactory. The intramuscular route of injection was used in all of these cases.

Some bacteriologic cures were obtained with amounts of penicillin smaller than 100,000 O.U. and administered in less than six hours. Single doses of 75,000 O.U., 50,000 O.U. or even 25,000 O.U. were likewise found to be adequate in some cases. However, this type of therapy is not to be recommended since the percentage of failures was high. The observation, that such subtherapeutic doses can cure individual patients, is consistent with laboratory findings that different gonococcus strains vary markedly in their susceptibility to penicillin.³

Clinical Changes

The following clinical changes were observed after penicillin therapy. The urethral discharge diminished in amount, or disappeared completely within a week or less in practically all of the cases studied. The cervical discharge, however, persisted in most cases throughout the entire follow-up period. In a very limited number of patients, the cervical discharge disappeared for a few days, but soon recurred. In general, it may be stated that the amount and character of the discharge observed in the urethra and cervix before and after penicillin treatment did not differ essentially from that observed in women receiving sulfonamide therapy.⁴

Adnexal Involvement

In 20 of the 34 patients in whom adnexal involvement was present, tenderness and thickening of the tubes or ovaries subsided within a few days after penicillin treatment. In 10 other patients suffering from acute exacerbation of chronic pelvic inflammatory disease, the acute symptoms and signs appeared to be improved by penicillin therapy. However, in these patients no essential changes were observed in the size or character of the adnexal masses which were present before therapy. In the remaining 3 cases, an exacerbation of the adnexal involvement was observed following the use of penicillin. One of the patients, without any adnexal disease prior to penicillin treatment, developed salpingitis following therapy. Within 1 to 2 weeks after penicillin treatment, the acute symptoms and signs of adnexal involvement disappeared in all 34 patients.

Gonococcal peritonitis, in the one patient reported, responded strikingly to 100,000 O.U. of penicillin; the same amount which was found necessary in less complicated cases. The patient who developed acute arthritis of the right elbow during the course of penicillin therapy recovered within a few days without any further treatment. The course of pregnancy in 6 patients was unaffected by penicillin.

There were 14 women who suffered from a concurrent infection of *Trichomonas vaginalis* which remained unchanged by penicillin therapy.

Clinical Follow-up

After their discharge from Bellevue Hospital, 81 of the total of 108 women were followed up at the Research Clinic of the Department of Health, City of New York, for an average period of 43.6 days during which an average of 3.5 examinations were performed. During the course of this follow-up, there were 15 women who were found to be gonococcus positive again after an average of 51.7 days and 3.4 examinations. Nine of these had originally suffered from adnexal involvement. The question arose as to whether these cases represented a relapse of their previous infection or new infections. Thirteen of the patients admitted new exposures, while 2 persistently denied the possibility of a new infection. Of these 15 women, 6 who were originally sulfonamide-resistant responded to one course of sulfathiazole therapy for their reinfection. Four, including the 2 who denied exposure, were cured by a second course of penicillin. The remaining 5 cases were delinquent.

It is difficult to decide whether these 15 cases represent instances of relapse or of reinfection. Among the hospitalized patients it was observed, that relapses after inadequate therapy always occurred within 24 hours after the administration of the penicillin. In the 15 women who became gonococcus positive during follow-up, reversals to positive occurred after an average of 51 days' observation. Thirteen of these admitted new exposures, the remaining two women were completely unreliable. Another fact which points to reinfection was that 6 patients in this group responded to one course of sulfonamides although they had previously been sulfonamide-resistant cases. In view of these facts, it is our impression that practically all 15 of these cases represent reinfections rather than recurrences.

Toxicity

One of the greatest advantages of penicillin therapy is the absence of any serious toxic symptoms in patients thus treated. The only complaint of the majority of these patients was a transitory numbness or pain following injection radiating from the site of injection in the gluteal region down to the thigh or ankle. Chills of a mild degree, rising temperature, a macular rash and generalized lymphadenopathy were observed in one patient, who suffered from a concurrent early syphilitic infection (Herxheimer reaction).

Comment

The total dosage of penicillin and the time-dose ratio are apparently the basic factors which determine a successful schedule of penicillin therapy. Our investigation was directed at evaluating the minimum effective dosage of penicillin due to the fact that the amount of penicillin available during the course of the study was very limited. Furthermore, we wanted to establish an effective time-dose ratio which could be used for the treatment of ambulatory patients. From our results thus far, it appears that a minimum total dosage of 100,000 O.U. of penicillin administered in 3 intramuscular injections at 3-hour intervals—an initial injection of 50,000 O.U. followed by 2 injections of 25,000 O.U. each—is a satisfactory treatment schedule which is completed within a period of 6 hours.

Although we have not yet encountered any instances of penicillin failure in our series, it is a possibility which cannot be eliminated at our present state of knowledge. Failure of penicillin might be due to two main factors: (1) A true resistance on part of the gonococcus strain to the bactericidal action of penicillin itself, the occurrence of which has not yet been proved; (2) the inability of penicillin to reach and act upon organisms which may be walled off in inaccessible foci of the genital tract.

It may be pointed out that a second course of penicillin treatment consisting of 4 single doses of 25,000 O.U. each, administered at 3-hour intervals has proved to be therapeutically effective in 9 patients who failed to respond to a first course of penicillin therapy.

The most difficult problem involved in this study of female gonorrhea is the establishment of definite cure. Clinical signs are of no appreciable value in its determination. Repeated bacteriologic examination, extended over a period of 2 to 3 months if possible, is the only means of establishing cure with any degree of certainty. The differentiation between relapse or reinfection after apparent cure is frequently impossible. History of new exposure, time of follow-up after treatment, number of examinations performed and final response or failure to a repetition of the original therapeutic schedule are factors which may aid in the clarification of this problem.

Summary and Conclusions

1. Various amounts of penicillin were used in the treatment of 108 adult female patients suffering from gonococcal infections. Of these, 101 had failed to respond to at least two courses of various sulfonamides; the remaining 7 patients showed a definite sensitivity to sulfonamide compounds.

2. Of the total of 108 patients, 99 promptly became bacteriologically negative after one course of penicillin treatment, and 9 by the administration of a second course of penicillin.

3. The results obtained by the administration of various amounts of penicillin point to the fact that a minimum total dosage of 100,000 O.U., injected intramuscularly in divided doses, is both necessary and sufficient for bacteriologic cure. The minimum total period of time required for successful therapy was found to be six hours.

4. Smaller doses of penicillin and shorter total time of treatment were adequate in individual cases, but this type of therapy cannot be recommended.

5. Urethral discharge following penicillin therapy disappeared within a week; cervical discharge was not appreciably affected in the majority of cases.

6. Acute symptoms and signs of adnexal involvement subsided within 1 to 2 weeks after penicillin treatment. There were 3 cases which had an exacerbation of the adnexal involvement immediately following the use of penicillin, and 1 patient who developed salpingitis following therapy.

7. After their discharge from the hospital, 81 of the total of 108 women were followed up for an average period of 43.6 days, during which an average of 3.5 examinations were performed.

8. Fifteen patients were found gonococcus positive after an average follow-up of 51.7 days. It may be assumed for various reasons that all these patients represent reinfections rather than recurrences.

9. No serious toxic symptoms appeared in this group of patients treated with penicillin.

References

1. Cook, E. N., Pool, T. L., and Herrell, W. E.: Further Observations on Penicillin in Sulfonamide-Resistant Gonorrhea, *Proc. Staff Meet. Mayo Clin.* 18: 433, 1943.
1. Strauss, Hyman: Cure by Penicillin Following Repeatedly Unsuccessful Sulfonamide Therapy in a Pregnant Woman With Gonorrhea, *Am. J. Obst. & Gynec.* 47: 271, 1944.
- Bloomfield, A. L., Rantz, L. A., and Kirby, W. M. M.: The Clinical Use of Penicillin, *J. A. M. A.* 124: 627, 1944.
- Barringer, Emily Dunning, Strauss, Hyman, and Horowitz, E. A.: Penicillin Treatment in Sulfa-Resistant Cases of Gonorrhea in the Female, *Ann. Meeting of the Medical Society of the State of New York*, May 10, 1944.
2. Cohn, Alfred, Studdiford, William E., and Grunstein, Isaak: Penicillin Treatment of Sulfonamide-Resistant Gonococci Infections in Female Patients; Preliminary Report, *J. A. M. A.* 124: 1124, 1944.
3. Cohn, Alfred, and Seijo, Irma: The in Vitro Effect of Penicillin, *J. A. M. A.* 124: 1125, 1944.
4. Cohn, Alfred, and Grunstein, Isaak: Gonorrhea in the Female. Bacteriologic and Clinical Aspects, *Am. J. Obst. & Gynec.* 48: 339, 1944.

THE TRANSMISSION OF PENICILLIN THROUGH THE PLACENTA*

A Preliminary Report

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A STUDY was started in May, 1944, to determine what place penicillin might have in obstetric therapeutics. The first problem consisted of finding out whether or not the placenta would offer a barrier to the passage of penicillin from the maternal circulation into the fetal blood supply. If penicillin could be detected in the fetal blood, it seemed important to determine the amount necessary to give the mother in order to obtain an adequate therapeutic concentration in the fetus.

Procedure and Findings

Amorphous penicillin, as the sodium salt, was placed in solution with normal saline in concentration of 5,000 units per cubic centimeter. Labors were closely observed in order to give an intramuscular injection of penicillin to each patient within a period of less than two hours before delivery. At the time of delivery, penicillin blood levels were obtained both from the antecubital vein of the mother and the umbilical vein of the infant. In a few patients, in which delivery did not occur within the first hour after injection, maternal blood levels were obtained one hour after administration of the penicillin and at the time of delivery.

The bacteriostatic level of penicillin varies with different strains of organisms. The test strain used in this study was *Staphylococcus aureus* 209, for which the minimum bacteriostatic blood level has been determined to be 0.02 Florey units per cubic centimeter.^{1, 2}

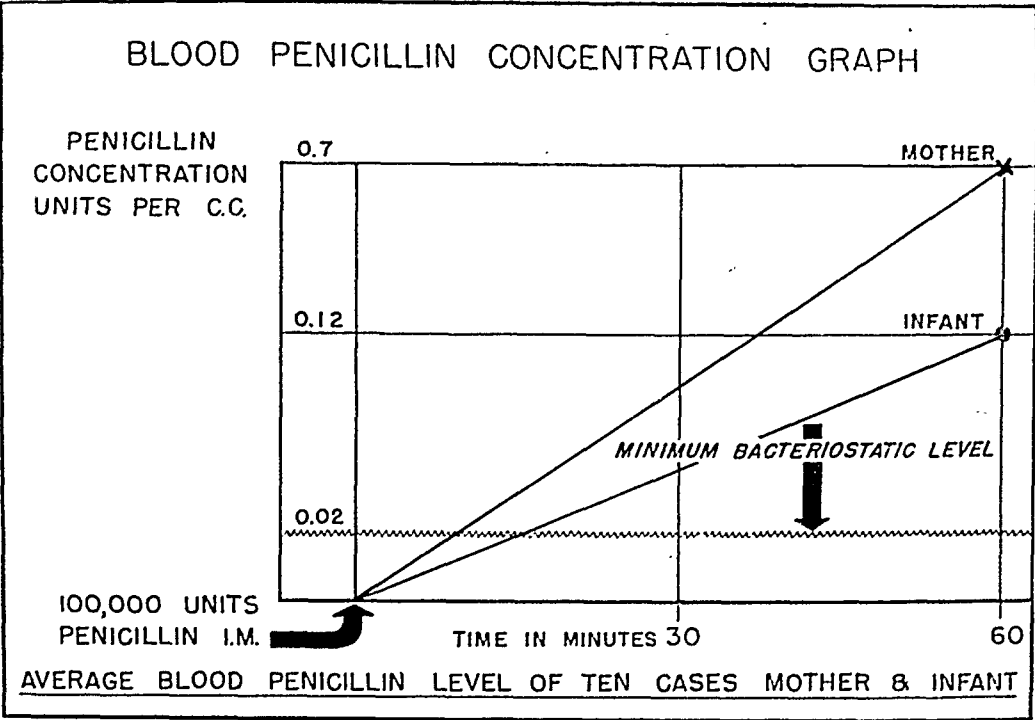
An initial dosage of 20,000 units was tried on one patient. Thirty minutes after intramuscular administration of penicillin to the mother, a penicillin level of less than 0.02 Florey units per c.c. was obtained from the infant cord. The maternal blood level at the time of delivery was 0.08 units per cubic centimeter.

Two patients were given 40,000 units of penicillin by intramuscular injections. Ineffective blood levels of less than 0.02 units per c.c. were obtained from the infants. The maternal levels were 0.08 units per cubic centimeter.

The dosage was then increased to a single 10 c.c. intramuscular injection of 100,000 units of penicillin (10,000 units per c.c.). With this dosage, observations were made on ten patients. Effective bacteriostatic levels were obtained in the fetal blood. The maternal levels ranged from 0.1 units per c.c. to 2.5 units per cubic centimeter. The fetal blood levels ranged from 0.02 units per c.c. to 0.2 units per cubic centimeter. A composite average of fetal and maternal penicillin blood levels is charted in Fig. 1. A complete record of maternal and fetal penicillin blood levels is given in Fig. 2.

*The opinions and views set forth are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

Fig. 1.



PENICILLIN BLOOD LEVELS						
PATIENT	DATE		BLOOD LEVEL MOTHER 1ST. HR.	TIME INTERVAL BET. INJ. & DEL.	BLOOD LEVEL MOTHER AT DEL.	BLOOD LEVEL FOETUS
M.B.	6-27-44	100,000 UNITS I.M. PENICILLIN	0.3 ^u /c.c.	1 hr. 45 min.	0.1 ^u /c.c.	0.06 ^u /c.c.
M.R	6-27			30 min.	0.3 ^u /c.c.	0.02 ^u /c.c.
W.M.S.	6-27			55 min.	0.6 ^u /c.c.	0.1 ^u /c.c.
A. C.	7-5			1 hr. 05 min.	0.20 ^u /c.c.	0.14 ^u /c.c.
K. P	7-6		1.24 ^u /c.c.	1 hr. 19 min.	0.3 ^u /c.c.	0.2 ^u /c.c.
R. B	7-11			1 hr. 17 min.	0.4 ^u /c.c.	0.14 ^u /c.c.
M. M.	7-17			1 hr. 45 min.	0.3 ^u /c.c.	0.154 ^u /c.c.
G. T.	7-18			58 min.	0.62 ^u /c.c.	0.14 ^u /c.c.
E. D.	7-18			25 min.	2.5 ^u /c.c.	0.14 ^u /c.c.
A. J.	7-18			1 hr. 06 min.	1.2 ^u /c.c.	0.14 ^u /c.c.

Fig. 2.

Discussion

Our results confirm the report of Herrell, Nichols, and Heilman,⁴ that 100,000 units of penicillin injected intramuscularly into the pregnant patient at term will result in an adequate bacteriostatic penicillin level in the fetal circulation. We have no data on the passage of penicillin through the placenta of the patient in the first or second trimesters of pregnancy. One patient, K. P., had positive blood serology, but a normal appearing placenta. Another patient, R. B., had moderately severe pre-eclamptic toxemia with multiple small placental infarcts.

The fact that penicillin passes from the maternal into the fetal circulation in effective concentrations suggests a wide therapeutic application of a relatively nontoxic agent for the control of penicillin susceptible infections which affect the mother and her unborn infant. Of these infections, syphilis should receive greatest consideration. If penicillin will eradicate syphilitic infections in the mother and fetus, it should replace the much more toxic arsenical preparations in the treatment of syphilis in pregnancy. Penicillin, given during labor to patients with known gonococcal infections, should reduce the incidence of postpartum gonorrheal salpingitis and gonorrheal ophthalmia neonatorum. The prophylactic use of penicillin in patients with prolonged rupture of the membranes should reduce puerperal infection in the mother and increase fetal resistance to intrauterine pneumonia. It seems that the factor of safety for mother and infant would be increased by substituting penicillin for the more toxic sulfonamides in the treatment of all penicillin susceptible infections complicating pregnancy.

We wish to express our appreciation to Lieutenant P. V. Wolley, Jr. (MC), USNR, Bacteriologist of the National Naval Medical Center, Bethesda, Md., for determining the penicillin blood levels.

References

1. Abraham, E. P., Chain, E., Fletcher, C. M., Florey, H. W., Gardner, A. D., Heatley, N. G., and Jennings, M. A.: *Lancet* 2: 177-188, 1941.
2. Hobby, G. L., Meyer, K., and Chaffee, E.: *Proc. Soc. Exper. Biol. & Med.* 50: 285-288, 1942.
3. Herrell, Wallace E., Nichols, Donald R., and Heilman, Dorothy H.: *J. A. M. A.* 125: 1003-1011, 1944.

THE ACTION OF VERATRONE ON BLOOD PRESSURE, URINE VOLUME AND UREA CLEARANCE IN THE TOXEMIAS OF PREGNANCY

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THE maintenance of normal kidney function in the toxemias of pregnancy is of utmost importance. Because the progression of pre-eclampsia is usually accompanied by a decrease in urinary output, many methods have been utilized in an attempt to promote the normal excretion of urine. At the present time, the administration of hypertonic glucose solutions to increase the blood volume through the withdrawal of extracellular water is the most effective method of accomplishing this purpose. There is no drug which may be used with any degree of success.

The positive water balance and the hypertension associated with pre-eclampsia and eclampsia are thought to be due, at least in part, to vascular spasm; thus, the use of a substance which will both lower blood pressure and relax the spastic vessels should be beneficial in the treatment of these conditions.

Veratrum viride was first used in the treatment of eclampsia by Barker about 1850; however, in the 1874 edition of his book *The Puerperal Diseases*, no mention of the drug is made except for its use in infections. Jewett, in 1887, reported a mortality rate of 27 per cent in 22 cases treated with veratrum, and Zinke¹ in 1911, was able to reduce his mortality rate from 34.4 per cent in 64 cases to 15.4 per cent in 26 cases by use of this preparation. Bryant² in 1935, reported a mortality of 10 per cent (121 cases), and in 1940,³ 1.7 per cent in 120 cases. In addition to veratrone, however, sedation, magnesium sulfate, glucose and induction of labor were liberally utilized.

Physiologic experimentation has revealed that the primary site of action is on the vagus center, stimulation of which is followed by slowing of the pulse and a fall in blood pressure, both being relieved by section of the vagi. Willson and Smith⁴ were able to demonstrate a direct peripheral vascular dilatation in animals. In these experiments, there occurred a drop in blood pressure without change in pulse rate and an increase in leg and spleen volume when the drug was injected into vagotomized dogs. The perfusion rate through isolated organs also increased when veratrone was injected into the perfusion system indicating that there is a direct dilating effect on the vessel wall.

Because little is known of the effects of this preparation on the vascular system in the human being, it seems desirable that its action be completely studied before its widespread use is again advocated. The results of the first of a series of studies on this problem are reported here.

Methods and Material

A total of 14 tests were made on prenatal patients, eight with essential hypertension, five with pre-eclampsia and one normal. Five of these subjects were again studied after delivery. All had been at complete bed rest for at least 24 hours prior to the test and all, except the normal, were on a pre-eclamptic diet (less than 2 Gm. of sodium chloride daily). Because of the constant oliguria or anuria associated with eclampsia, it was impossible to study this group.

Early on the morning of the test, the patients were given 200 c.c. of water by mouth; this was repeated at half-hour intervals and in all instances, a total of at least 1,600 c.c. of fluid was taken. A control urea clearance was begun at the end of the first hour, and at the completion of the control test, veratrone was administered subcutaneously, the initial dosages varying from 0.5 to 0.75 cubic centimeters. If after thirty minutes there had occurred no marked change in blood pressure another injection, usually 0.25 c.c., was given. The subsequent urea clearance periods were of at least 30 minutes' duration.

All urine specimens were collected by catheter at half-hour intervals, the bladder being emptied each time, and the amount carefully measured.

Results

Effect on Pulse Rate and Blood Pressure.—In most instances, the administration of the drug was followed by a reduction in pulse rate of at least 12 beats per minute (the lowest rate observed was 40) and a fall in blood pressure. In four cases, all with essential hypertension, the pulse rate either remained the same, or rose despite the fact that the blood pressure was decreased. Although the fall in blood pressure usually occurred coincidentally with the slowing of the pulse, this association was less apparent as the blood pressure returned to the preinjection level. In most instances, the pulse rate reached its original rate while the blood pressure remained low. No irregularities in heart action were observed. The depression of blood pressure was obtained more easily in the patients with pre-eclampsia than in those with essential

hypertension. In the former group, it was necessary to repeat the injection of veratrone only twice (40 per cent), while in the latter, subsequent dosages were necessary seven times (87 per cent) to produce a distinct fall in pressure. The maximum drop occurred in an average of two and one-half hours after the initial injection and was comparable for each group. The fall averaged 48/27 mm. Hg in those with hypertension, and 51/38 mm. Hg in those with pre-eclampsia from initial pressures averaging 168/115 for the former, and 163/116 for the latter.

The average time before the blood pressure returned to the control level exceeded six hours for all patients; in one patient with essential hypertension the blood pressure had not returned to the preinjection level in ten hours, and in one pre-eclamptic in 15 hours. The maximum drop was followed by a gradual rise to the control level.

More of the drug was necessary in the normal patient to effect an alteration in blood pressure than in the patients in whom the pressure was elevated. In this instance, after a total dosage of 1 c.c. of veratrone, there occurred a diminution from 130/80 to 100/60 mm. Hg with a return to normal within two hours after the most marked depression (Fig. 1).

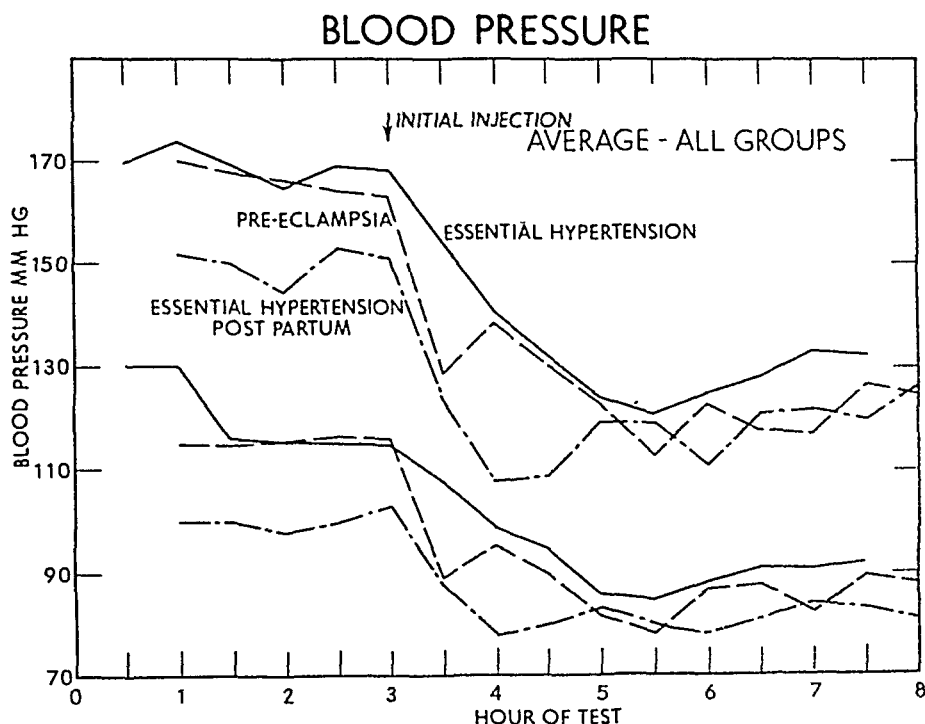


Fig. 1.—The effect of veratrone on blood pressure in pre-eclampsia and essential hypertension before delivery, and in essential hypertension during the postpartum period.

Effect on Urine Volume.—Although each patient ingested at least 1,200 c.c. of water during the control period, a definite difference in output was noted for the hypertensive patients as compared with those with pre-eclampsia. In seven of the former group, there occurred a gradual increase in urinary output during this period of hydration to a peak at the time of administration of the drug. The urine volume of the pre-eclamptic patients was altered only slightly by the administration of water by mouth. This observation is illustrative of one of the important differences in kidney function between the two conditions.

Following the injection of veratrone, a definite diminution in urine volume was noted in both groups; however, this change was much more marked in the patients with pre-eclampsia. In these subjects, the maximum depression occurred in 3½ hours when the volume per minute averaged only 4.3 per cent of that at the time the drug was given.

Of these five patients, all except one, had a urine output greater than 3 c.c. per minute during the control period. In each instance after

injection of the drug, this was decreased to less than 1 c.c. per minute for periods varying from 30 minutes to 4 hours. In four of the five patients, a complete suppression of urine occurred; of the latter one produced no urine for $\frac{1}{2}$ hour, two for one hour, and one for two hours.

The most marked depression of kidney function in the subjects with essential hypertension was noted two hours after the injection, at which time the output averaged 47 per cent of the control level. In only four patients was the urine output decreased below 1 c.c. per minute; two for 30 minutes; one for one hour, and one for $1\frac{1}{2}$ hours. In only one did urine excretion cease completely, the anuria lasting only $\frac{1}{2}$ hour. In the normal patient, the urine volume decreased to less than 1 c.c. per minute in one thirty-minute period during the most marked depression of blood pressure (Fig. 2).

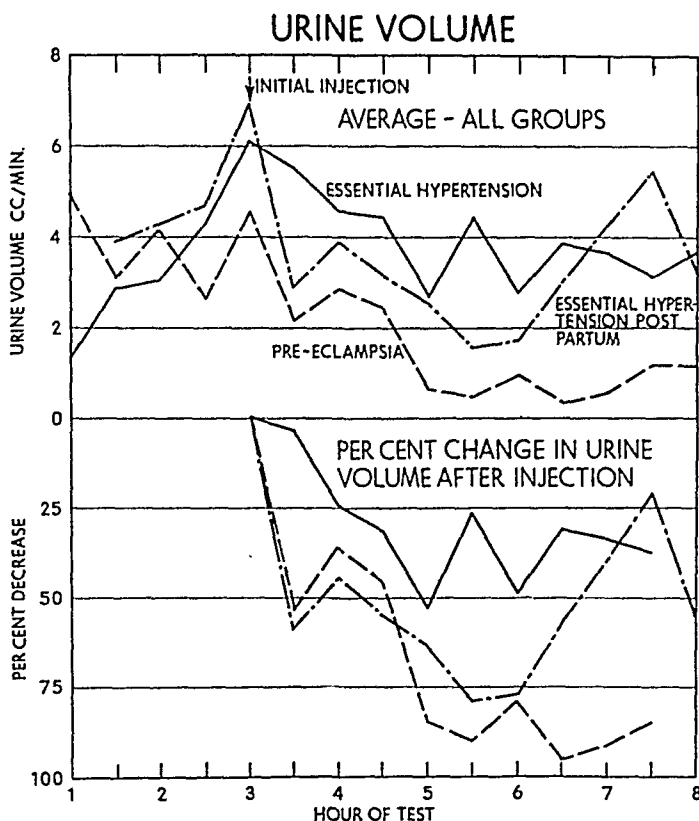


Fig. 2.—Effect of veratrone on urine volume. The upper chart shows the average urine outputs in c.c./min. for the three groups. The lower chart shows the percentage reduction in urine volume as a result of the injection of veratrone. The average urine volume in c.c./min. for the last half hour of the control period was taken as the base line and the reduction calculated from this figure.

Effect on the Excretion of Urea.—The administration of veratrone was followed by a definite reduction in urea clearance. This reduction appeared to be directly related to the diminution in blood pressure, since it became progressively more pronounced as the latter decreased, and improved with the return of the pressure to the original level. For the patients with pre-eclampsia (Figs. 3 and 4) the urea clearance just preceding the injection averaged 41 c.c. of blood cleared per minute; this was reduced in $2\frac{1}{2}$ hours to a minimum of 5 c.c. per minute. The clearance remained below 20 c.c. per minute for a total of two hours. Although subsequent urine volumes were not greatly increased, there occurred a rise in the urea clearance starting three hours after the drug had been given to an average of 35 c.c. per minute two hours later.

The decrease in urea clearance also was noted in the hypertensive patients (Figs. 3 and 4) but with the exception of one-half-hour period, was much less marked. The control clearance of 53 c.c. per minute was reduced to a low of 11 c.c. per minute in $2\frac{1}{2}$ hours; however, in direct

contrast to the pre-eclamptic patients, the preceding and succeeding figures were 33 and 34 c.c. per minute, respectively. During the period at which the clearance was at its lowest, the urine output was only 26 per cent below the control level.

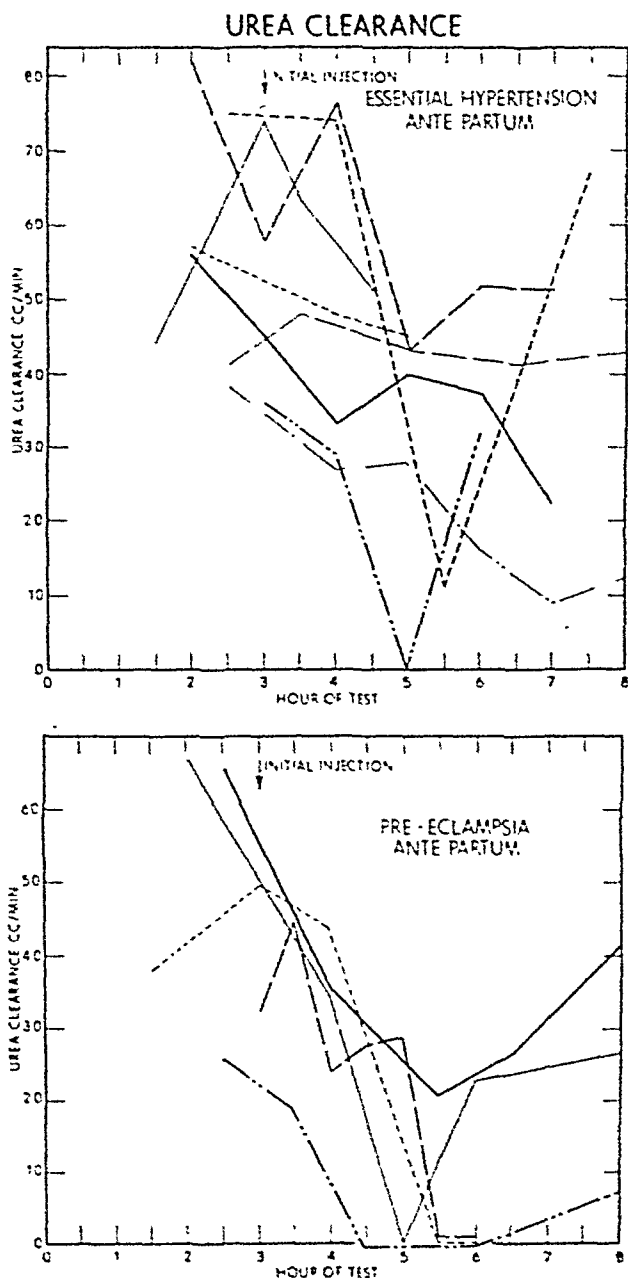


Fig. 3.—Effect of veratrone on urea clearance. The two charts showing the alteration in urea clearance in individual cases show the more marked drop in excretion in pre-eclampsia as compared with essential hypertension.

No significant alteration occurred in the normal patient.

In the hypertensive patients the figure for U/B ($\frac{\text{urine urea nitrogen}}{\text{blood urea nitrogen}}$) fell as the urine volume increased during the period of hydration. No significant alteration in this figure followed the injection of veratrone. Little change in U/B was observed during the control period in the pre-eclamptic patients, probably directly correlated with the failure of increased fluid intake to alter markedly the urine output. Following the injection, this figure fell to 0 in those patients in whom the urine output was completely depressed; two rose above the control level with recovery of function, one from an initial figure of 10 to 24, and one from 15 to 38. In the others, no great change was noted.

Effect of Delivery.—The postpartum response to veratrone in a patient who had had pre-eclampsia was essentially the same as that during the

pregnancy. Although the control urine volume was higher after delivery, there occurred a pronounced diminution in output in response to injection of the drug; *complete suppression was not obtained despite the fact that the lowest blood pressure in the postpartum test was below that produced during the previous examination.* In this same patient, a period of urinary suppression lasting two hours had been precipitated by the drug during pregnancy.

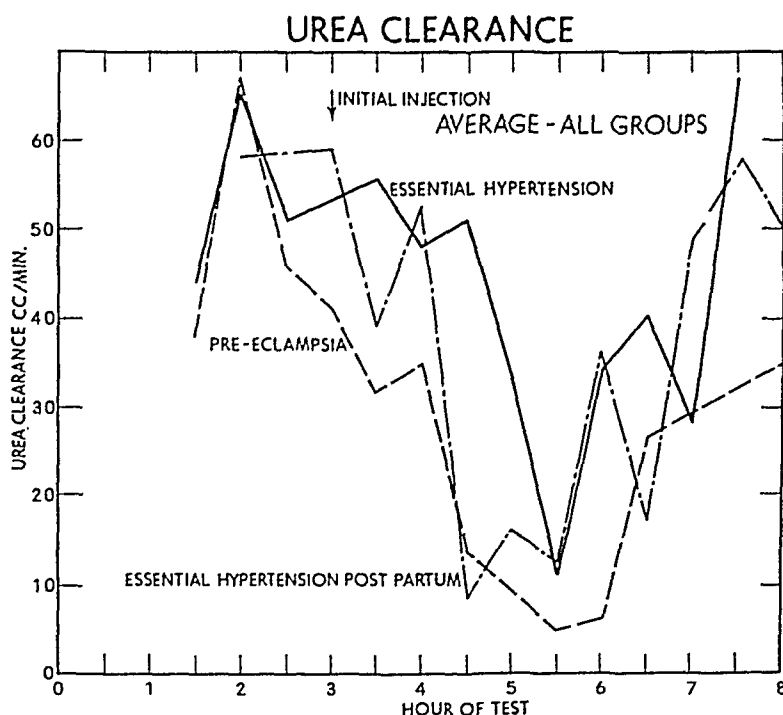


Fig. 4.—Average fall in urea clearance in pre-eclampsia and essential hypertension before delivery, and in essential hypertension during the postpartum period as a result of injection of veratrone.

The postpartum results in four patients with essential hypertension differed from those before delivery. The blood pressure drop averaged 44/25 mm. Hg and was noted one hour after the drug had been given. The average diminution in urine volume was greater than that of the hypertensive patients before delivery, but less than the figures obtained for those with pre-eclampsia. No subject failed to excrete urine even during the most marked depression of blood pressure. Recovery of kidney function occurred more rapidly after delivery than in either of the groups during pregnancy. The urea clearance decreased rapidly to its lowest point 1½ hours after the drug had been injected, and remained below 20 c.c. per minute for 1½ hours, an hour longer than the hypertensive patients during pregnancy. Little change was observed in the U/B.

General Reactions.—Most patients complained of burning at the site of the injection, but no marked local reaction developed in any case. Burning in the throat likewise occurred frequently. Four of the five pre-eclampsics vomited when the blood pressure dropped, but in only one of the hypertensive patients did this occur.

Discussion

Improvement during the course of pre-eclampsia only follows restoration of normal kidney function, and in the severe cases, this may be difficult or impossible to accomplish before delivery. Mere reduction of blood pressure is relatively unimportant in promoting the desired effect, since postpartum diuresis usually is established while the blood pressure remains elevated. It has been shown by McGee³ that when

intravenous sodium amytal is used to control eclamptic convulsions, hypotension and anuria may result. That the latter is a result of lowering of blood pressure is demonstrated by the fact that kidney function may be re-established following the injection of ephedrine to increase arterial tension. Warthin and Thomas⁶ were able to reduce both blood pressure and renal blood flow in hypertensive dogs by the intraperitoneal injection of pentobarbital.

Because of the constant association of vascular spasm with pre-eclampsia, it seems likely that the changes which occur may be at least in part, a result of the diminution in caliber of the vessels. That there are no permanent changes in the vessel walls, is suggested by the fact that recovery from pre-eclampsia is complete without demonstrable alteration in the cardiovascular system. A drug which relieves vessel spasm should be of value as an addition to the treatment of this condition. The observations reported here demonstrate without question that veratrone reduces the blood pressure in toxemic patients, and we know from animal experiments, that there is a direct vasodilating effect. The direct action on blood vessels without interference from the vagus cannot be measured in the normal human being; however, the fact that the return of the pulse rate to its original level was not necessarily accompanied by an elevation in blood pressure, suggests that there is a vascular effect other than that through the vagus nerves. In spite of the fact that the blood pressure was depressed to normal levels and that vascular spasm was reduced, the kidney function was not only unimproved, but usually was decreased to a dangerously low point. Thus, we may conclude that vascular spasm and hypertension alone are not responsible for the functional changes associated with pre-eclampsia.

The differences in response to the administration of veratrone in the patients with essential hypertension as compared to those with pre-eclampsia may be explained by differences in the vessel walls. In both pre-eclampsia and early essential hypertension, the changes are the result of vascular spasm, but in the latter group, there occurs a progressive structural alteration in the blood vessel walls. Vascular dilatation and a fall in blood pressure in pre-eclampsia are easily obtained because of the lack of organic change, and the same holds true for early essential hypertension. In the latter group as the vascular sclerosis increases, complete relaxation of the vessel walls becomes more difficult to achieve and the response is less marked.

The excretion of both water and solids by the kidney is dependent upon normal blood flow through the renal vessels, normal glomerular filtration and normal tubular reabsorption. Alteration in any of these factors may be reflected either in a change in volume of urine excreted, or in its chemical content. Although the fall in blood pressure in the cases studied did not reach levels low enough to suppress kidney function in normal individuals, the direct association of decreased urinary output with decreased blood pressure makes this factor seem the most likely cause. In one patient with pre-eclampsia, however, a small initial dose of veratrone depressed the blood pressure only to 130/90 from 160/110, but the urine volume decreased about 50 per cent. Complete study of glomerular filtration and renal blood flow before and after ad-

ministration of veratrone is necessary before the exact mechanism by which the depression of renal function is produced can be determined.

Conclusions

1. The effects of the administration of veratrone to patients with both pre-eclampsia and essential hypertension during pregnancy and after delivery were studied.

2. The administration of the drug was followed by a decrease in pulse rate and a marked fall in blood pressure. This response was obtained more readily in the patients with pre-eclampsia than in those with essential hypertension.

3. Coincidental with the fall in blood pressure, there occurred a diminution both in urine volume and in urea clearance which likewise was more marked in pre-eclampsia.

4. The changes in kidney function are probably the combined result of the fall in blood pressure and an alteration in renal vascular dynamics.

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References

1. Zinke, E. G.: *Am. J. Obst.* 63: 217, 1911.
2. Bryant, R. D.: *AM. J. OBST. & GYN.* 30: 46, 1935.
3. Bryant, R. D., and Fleming, J. G.: *J. A. M. A.* 115: 1333, 1940.
4. Willson, J. R., and Smith, R. G.: *J. Pharmacol. & Exper. Therap.* 79: 208, 1943.
5. McGee, W. B.: *J. M. A. Alabama* 5: 4, 1935.
6. Warthin, T. A., and Thomas, C. R.: *Bull. Johns Hopkins Hosp.* 72: 203, 1943.

THIAMIN STATUS DURING PREGNANCY

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THERE is evidence that the thiamin status of an individual can be determined by measuring the twenty-four-hour output of thiamin in the urine.¹⁻³ This finding is dependent upon the fact that when the individual takes approximately the same diet day after day, there is a consistent urinary excretion of thiamin. Melnick³ has shown that if a normal adult consumes a well-balanced diet including 860 micrograms of thiamin daily, the average 24-hour urinary excretion of thiamin will be 200 micrograms. In contrast to this good thiamin status when taking a normal diet, he shows further that, when an inadequate diet of 260 micrograms thiamin intake daily is continued for 23 days, the 24-hour urinary excretion fell to 25 micrograms. Similar information regarding the thiamin status can be obtained by giving a test dose of thiamin by mouth or parenterally, and measuring the amount of thiamin later excreted in the urine during a specified time. A third method for finding the thiamin status is to establish excretion peaks as carried out by Lockhart.⁴ By this method the basal excretion of thiamin is first

established for an eleven-hour period. The following day, a test dose of thiamin is given. On successive nights, these doses are progressively increased until the urine analysis shows that the excretion peak is passed. The excretion peak is the point at which the highest proportion of the administered thiamin is excreted.

The first method as afore-mentioned was used for this report and presents the urinary excretion values of thiamin chloride in normal pregnant women. Twenty-four-hour urine specimens were collected from two groups of patients. The first group served as controls and took no extra thiamin in addition to the diet, while the second group took daily additions of thiamin chloride by mouth. The amounts of thiamin added varied from 0.75 mg. to 1.5 mg. daily as indicated in Table I. These patients were seen in private practice throughout pregnancy and consumed a well-balanced diet including milk, cheese, eggs, meat, 2 leafy vegetables daily, fruits and cereals. All the patients studied gave birth to normal, well-developed and well-nourished infants with the exception of one twin pregnancy, in which case, the first twin was stillborn. The blood pressure readings and the routine urine examinations showed no abnormal findings. The total number of patients studied and here reported was 42, twenty-nine of whom were primiparas. On these patients 154 separate tests for thiamin excretion were carried out.

Technique of Procedure

All patients were given written as well as verbal instructions for the collection of the 24-hour urine specimens. The specimen was accumulated in a previously prepared gallon bottle containing 20 c.c. of 10 per cent sulfuric acid, thoroughly mixed and measured. An aliquot portion was then sent to the Maternity Hospital Laboratory, Cleveland, Ohio, for the thiamin determination. The determinations were made by the fluorescent method as described by Wang and Harris,⁵ in which the thiamin is oxidized by potassium ferricyanide in an alkaline solution to thiochrome and read in the light of a mercury lamp under a suitable filter. Standards were prepared by adding known amounts of thiamin, oxidized to thiochrome, to blanks prepared from each urine sample. A number of precautions suggested by Dr. C. A. Mills⁶ was observed, especially that of using only Pyrex glass throughout, and redistilling all the reagents. Recoveries were determined with each specimen by adding small amounts of thiamin to portions of the original urines.

In Table I, are listed two groups of normal pregnant patients. Group I serves as a control since no extra thiamin chloride was added to the diet, while Group II includes the patients that took a specified amount of thiamin daily throughout the period of gestation. The average urinary excretion value of thiamin for each group is presented for each trimester of pregnancy. In the Control Group the results indicate a tendency for the excretion of thiamin to decrease toward the end of pregnancy. In other words, as pregnancy advances the demand for thiamin increases, and this finding coincides with the conclusion of Lockhart⁴ who used excretion peaks following test doses of thiamin.

In Table II, are listed two cases which demonstrate that multiple pregnancy or prolonged vomiting lead to a diminution in the urinary excretion of thiamin chloride. In the first case, the need for thiamin chloride is greater than in single pregnancies, while in the second case, the dietary intake of thiamin is lowered by the vomiting and this in turn leads to lowered excretion.

TABLE I.—AVERAGE 24-HOUR URINARY EXCRETION OF THIAMIN CHLORIDE IN
NORMAL PREGNANCY
MEANS—WITH STANDARD ERRORS—GIVEN IN MICROGRAMS

	NO. PA- TIENTS	NO. TESTS	1ST TRI- MESTER	2ND TRI- MESTER	3RD TRI- MESTER
Group I	8	12	286 ± 37		
Normal diet — no thiamin added	10	24		263 ± 25	
	10	17			249 ± 41
Group II	4	4	478		
Normal diet + 0.75 mg. thiamin daily	16	41		620 ± 44	
	17	39			483 ± 27
Normal diet + 1.50 mg. thiamin daily	0	0	-----		
	4	8		932 ± 139	
	3	4			1131

TABLE II.—AVERAGE 24-HOUR URINARY EXCRETION OF THIAMIN CHLORIDE IN
MULTIPLE PREGNANCY AND PROLONGED VOMITING
MEANS GIVEN IN MICROGRAMS

	PA- TIENTS	NO. TESTS	1ST TRI- MESTER	2ND TRI- MESTER	3RD TRI- MESTER
Twin Pregnancy	B.R.	0	-----		
*Normal diet + 0.75 mg. thiamin daily	B.R.	1		270	
	B.R.	1			335
Prolonged vomiting	J.C.	1	473		
*Normal diet + 1.50 mg. thiamin daily	J.C.	2		516	
	J.C.	0			-----

*Normal in quality, intake varied with conditions of patients.

Comment

Although the total number of patients studied is not large, yet two facts are evident and worth emphasizing. First in importance is the finding that a well-balanced diet does give the normal pregnant women a good thiamin status. In the Control Group of patients in which no thiamin was added to the diet, the average excretion of thiamin for each trimester was well over 200 micrograms, which Melnick³ gives as the amount of thiamin excreted on a normal diet. If thiamin is added daily in addition to the diet, the 24-hour urinary excretion is increased accordingly. For example, the small addition of 0.75 mg. daily approximately doubled the urinary excretion of thiamin over that of the controls. Therefore, excessive doses of thiamin to normal pregnant patients who eat a well-balanced diet are not justified.

In this connection it is well to remember that the requirement for thiamin is increased during normal pregnancy. Hoffman⁷ pointed out in 1924, that in his experience in Canton, China, beriberi developed more frequently in women during pregnancy than at other times. Also that beriberi tends to recur with recurring pregnancies. The recommendation of the National Research Council⁸ is that the diet should contain 1.8 mg. thiamin daily during pregnancy. Although the diets taken in this present experiment were not analyzed for thiamin content, yet the urinary excretion shows good thiamin status from diet alone.

The second fact that this report shows is that multiple pregnancy or prolonged vomiting lowers the urinary excretion of thiamin. In

Table II, the patient, B.R., who had a twin pregnancy, took a daily addition of 0.75 mg. thiamin. During the second and third trimesters, the 24-hour urinary excretion of thiamin was only 270 and 335 micrograms, respectively, while the normal, single pregnancy patients, who took the same daily addition of thiamin showed an excretion of 619 micrograms for the second trimester, and 483 micrograms for the third. Thus, this case of twin pregnancy showed a definitely diminished excretion of urinary thiamin in 24 hours. The second patient listed in Table II, J.C., continued to vomit 2 or 3 times a day from the sixth week through the first trimester of her gestation. Although she took a daily oral dose of 1.5 mg. of thiamin, the urine test for thiamin at the end of the first trimester revealed only 473 micrograms. Soon after this test the vomiting subsided, but the appetite remained poor and a second test done during the second trimester revealed that the thiamin excreted was 330 micrograms. The group of normal pregnant patients, who took a similar daily dose of thiamin, showed an excretion for the same period, i.e., the second trimester, of 932 micrograms. Therefore, in multiple pregnancy or prolonged vomiting, moderate daily doses of thiamin are not only justified but probably necessary, if a good thiamin status is to be maintained. The vitamin B intake could be increased easily by taking special high vitamin B bread as reported by Free⁹ in 1940.

Dexter and Weiss¹⁰ state that in toxemia of pregnancy, so far as we know today, the vitamin requirement increases no more than in normal pregnancy. Nixon¹¹ in 1942, however, found that in eclampsia the amount of B₁ excreted in the urine is significantly lower than in normal pregnancy, also the concentration of thiamin in the placenta was significantly below that of the placenta from normal cases. Siddall¹² in 1938, suggested a possible etiological relationship between vitamin B deficiencies and pre-eclampsia and eclampsia. In this connection, King's¹³ report from Hongkong in 1941 is significant. He observed 42 cases of eclampsia, 19 (45 per cent) of which were complicated by avitaminosis B₁. Of 13 deaths, 11 had this complication. Thus, in 85 per cent of eclampsia deaths, there was the double lesion of eclampsia and avitaminosis B₁. Missett¹⁴ observed that the incidence of late toxemia is definitely increased in cases having nausea and some vomiting in the first trimester; 41 per cent of multiparas and 51 per cent of primiparas, who experienced this form of early toxemia, being toxic in the last trimester. He also found that those who had moderately severe vomiting during the early months were even more liable to late toxemia. The incidence was 56 per cent of multiparas, and 57 per cent of primiparas. Therefore, he suggests the likelihood that the occurrence of late toxemia is indeed proportional to the severity of its early manifestations. Thus, in the vomiting of pregnancy great care should be exercised to maintain a good thiamin status, and parenteral injections of thiamin may be necessary.

Summary

1. This report is a study of the thiamin status of normal pregnant women, as determined by measuring the 24-hour urinary excretion of thiamin chloride. Forty-two patients were observed, and 154 tests for thiamin excretion were made.

2. The control group took no daily additional thiamin chloride and the average 24-hour urinary excretion during pregnancy was as follows: first trimester, 286 micrograms, second trimester, 263 micrograms, and third trimester, 249 micrograms.

3. The daily addition to the diet of a small oral dose of thiamin, namely, 0.75 mg., approximately doubled the excretion value over the control group.

4. Lowered amounts of thiamin chloride in the urine may be caused by prolonged vomiting, poor appetite, or multiple pregnancy.

References

1. Harris, L. J., and Leong, P. C.: *Lancet* 1: 886-894, 1936.
2. Wang, Y. L., and Yudkin, J.: *Biochem. J.* 34: 343-352, 1940.
3. Melnick, Daniel: *J. Nutrition* 24: 139-150, 1942.
4. Lockhart, H. S., Kirkwood, Samuel, and Harris, R. S.: *AM. J. OBST. & GYNEC.* 46: 358-365, 1943.
5. Wang, Y. L., and Harris, L. J.: *J. Biochem.* 33: pt. 2, 1356, 1939.
6. Mills, C. A.: Cincinnati General Hospital, private communication.
7. Hoffman, J. A.: *Chinese M. J.* 38: 987-993, 1924.
8. National Research Council, Committee on Food and Nutrition, Washington, 1941.
9. Free, A. H.: *Cereal Chemistry*, 17: No. 6, 1940.
10. Dexter, Lewis, and Weiss, Soma: *Preeclamptic and Eclamptic Toxemia*, Boston, 1941, Little, Brown & Co., p. 375.
11. Nixon, W. C. W., Wright, M. D., and Fieller, E. C.: *Brit. M. J.* 1: 605-607, 1942.
12. Siddall, A. C.: *AM. J. OBST. & GYNEC.* 35: 662-667, 1938.
13. King, Gordon: Quoted by Nixon.¹¹
14. Missett, J. V.: *AM. J. OBST. & GYNEC.* 27: 697, 1934.

CARCINOMA OF THE OVARY TREATED PREOPERATIVELY WITH DEEP X-RAY*

Report of Three Cases

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THE treatment of cancer of the ovary is notoriously unsatisfactory. Probably less than 10 per cent of the solid infiltrating type and 40 per cent of the papillary adenocarcinomas survive five years. While the poor results are due in part to the tardiness in applying therapy, nevertheless, they have stimulated the search for improvement in the handling of these cases as we find them. Without exception, all who have studied the problem agree that in the treatment of carcinoma of the ovary, excision is the procedure of choice. Radiation for these cases is not so well established. Some support its use as an adjunct to operation, while others admit no benefit from radiation and assert that it can cause harm. This report of three inoperable cases of carcinoma of the ovary which were treated with deep x-ray therapy and were later found to be operable is presented as evidence that x-ray treatment may, in some cases, affect the course of the disease.

It is difficult to accurately appraise the effects of radiation. It is apparent that there was some effect upon the growth; although no great amount of destruction was noted. The effect was sufficient, however, to permit the removal of the mass later on.

*Presented at a meeting of the New York Obstetrical Society, May 9, 1944.

Whether these cases are isolated curiosities, or whether similar effects might be more frequently obtained can only be determined by further experience. The prevailing practice in ovarian neoplasms is to operate, to remove as much of the mass as possible even though large residual carcinomatous masses are left in situ, and then to employ x-ray. The generally unsatisfactory results following this treatment might make justifiable the planning of the treatment of papillary growths when not removable along the lines employed in the cases reported here.

A study of previous experiences in the use of radiation, follows along two lines, the statistical and the direct observation of individual cases. Statistical study is unsatisfactory mostly because of the great variation in standards of microscopic criteria, extent of disease, thoroughness of operation and follow-up interval.

Ford¹ found x-ray valuable after surgery and as a palliative measure when the condition was inoperable. Montgomery and Farrell² thought that radiation lessened pain and edema in addition to prolonging life. They reported the use of postoperative x-ray in 22 cases of ovarian cancer and found that all their cures were in the papilliferous type. They regarded it as important to consider the histologic diagnosis, grade of malignancy, degree of operability and radiation factors. Kean³ also favored postoperative x-ray. He found that it prolonged life and thought that it should be given even in hopeless cases as a palliative measure. Taylor and Greely⁴ reviewed the factors influencing end results in 138 cases of carcinoma of the ovary. They found that postoperative x-ray was especially useful in a limited number of the cases studied. Schmitz⁵ recommended x-ray postoperatively and suggested, that if the tumor was large and inoperable and ascites was present, the fluid be removed before deep x-ray was administered.

Harris and Payne⁶ in reporting 38 cases of carcinoma of the ovary found x-ray to be valuable as a postoperative measure. In addition, the following case, similar to the ones I am reporting, was cited: "An operation was begun, but the tumor was so far advanced that to continue the operation was thought inadvisable. A biopsy was taken which showed papillary cystadenocarcinoma of the ovary. The patient was given deep x-ray therapy, her condition seemed to improve and 33 months later she was operated upon again. At the time the report was given she had been well for five years."

Neither Lynch⁷ nor Meigs⁸ were enthusiastic regarding the use of radiotherapy in the treatment of carcinoma of the ovary. Goodall⁹, in a recent article, stated that cure or arrest of progress could not be expected from deep x-ray treatment alone, and that it occasionally caused harm by degeneration.

Deep x-ray as a preoperative measure is not a new procedure. Walthard and Heyman, as quoted by Geist¹⁰, have treated inoperable cases, which afterward became operable, with x-ray. In a series of 38 cases of carcinoma of the ovary, Marchetti¹¹ reported eight cases as having had an exploratory laparotomy and biopsy followed by roentgen therapy and a second operation. His conclusion was: "Unquestionably x-ray rendered operable a good part of previous inoperable cases in this group." Seven of these eight patients died with an average duration of life of seventeen months. One was alive twelve months after the second operation when the report was made.

Report of Cases

Three cases are presented in which the history and physical examination were comparable. In each instance, because of the size of the growth, density of adhesions, extent of infiltration and the apparently

hopeless outlook, the original operator did not remove the pelvic organs. A biopsy was taken and deep x-ray therapy was given which obviously caused the masses to become smaller and more movable and the implants on the peritoneum to shrink. Several months after the first operation, a second operation was performed in each case and at this time the neoplastic tissue and affected organs were removed. Two of the patients are still alive and apparently well after twelve and eight years. The third patient died of a carcinoma, thought to be unrelated, five years after the original operation.

CASE 1.—Mrs. E. S., Unit No. 348632, was admitted to Sloane Hospital for Women because of enlargement of the abdomen. She was operated upon on August 15, 1932. On opening the abdomen, it was found to contain a large quantity of straw-colored fluid and the pelvis and lower abdomen were filled with a granular, cauliflower-like mass the size of a six months' pregnancy. Numerous implants were noted on the parietal and visceral peritoneum,; the liver and epigastric regions were thought to be unaffected. As the condition was deemed inoperable, a biopsy was taken and the abdomen closed.

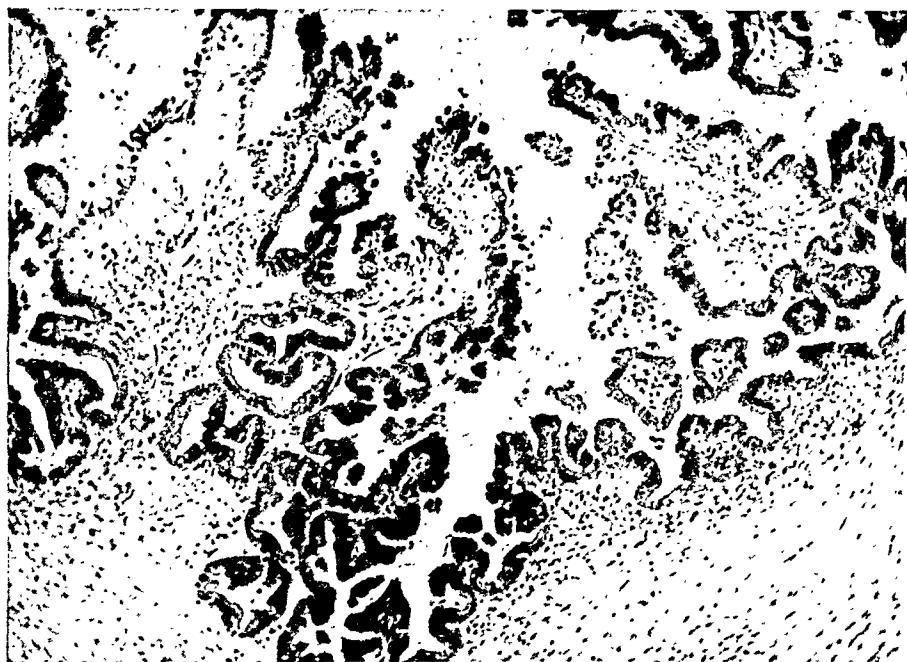


Fig. 1.—Sloane Hospital Pathology No. 6343 (Mrs. E. S.) shows microscopic disappearance of ovarian tumor tissue before radiation.

Microscopic Examination: (Fig. 1.) The epithelium in places was arranged in a single layer and was low cuboidal in type. In other places, many papillary folds were seen and the epithelium was high cylindrical in shape with basal nuclei. In some folds the cells were closely packed and formed irregular masses on the surface. The nuclei showed polymorphism varying in size, shape and staining quality. Many mitotic figures were visible. Numerous fibroblasts were seen in the supporting structure. Although the epithelium grew downward and in places formed alveolar-like spaces, the basement membrane was intact.

Diagnosis: Papillary cystadenocarcinoma of the ovary.

Deep x-ray therapy was instituted as a palliative and possible therapeutic measure. Between August 19, and September 16, 1932, inclusive, twenty-one exposures were given to the pelvic region through two fields, one anterior and one posterior, each measuring 20 cm. by 20 centimeters.

Each exposure was as follows: Kilovolts, 180, Anode skin distance

50 cm. Filter 0.55 mm. copper and 1.0 mm. aluminum. Total, 1,500 r. per field.

Also between December 28, 1932, and February 3, 1933, twenty exposures were given to the pelvic region through three fields, one anterior and two posterior each measuring 20 cm. by 25 centimeters.

Each exposure was as follows: Kilovolts, 180, Anode skin distance 50 cm. Filter 0.55 mm. copper and 1.0 mm. aluminum, Total, 1,700 r. per field.

The patient was examined in the Follow-up Clinic, one month after completing the second series of deep x-ray, the mass was thought to be smaller and more movable and a postoperative ventral hernia was noted. It was decided to perform another laparotomy with the hope that the tumor could be removed and the hernia repaired. On March 17, 1933, seven months after the first operation, a supravaginal hysterectomy and bilateral salpingo-oophorectomy were done. Upon opening the abdomen, the peritoneal implants were found to have entirely disappeared. A small amount of ascitic fluid was present and one whitish plaque was seen beneath the old scar. The pelvis and lower abdomen were filled with an irregular-shaped mass the size of a five months' pregnancy. There were a number of peritoneal adhesions in the pelvis. The uterus was normal in size. Both ovaries were cystic and in several areas papilliferous excrescences extended through the surface. In addition to cauliflower-like masses of tissue, some of the cysts contained a lemon-yellow thin fluid and others contained a thick brownish mucoid material. The right ovary measured 17.5 by 9.5 by 7 cm., and the left ovary measured 16 by 11 by 9 centimeters.

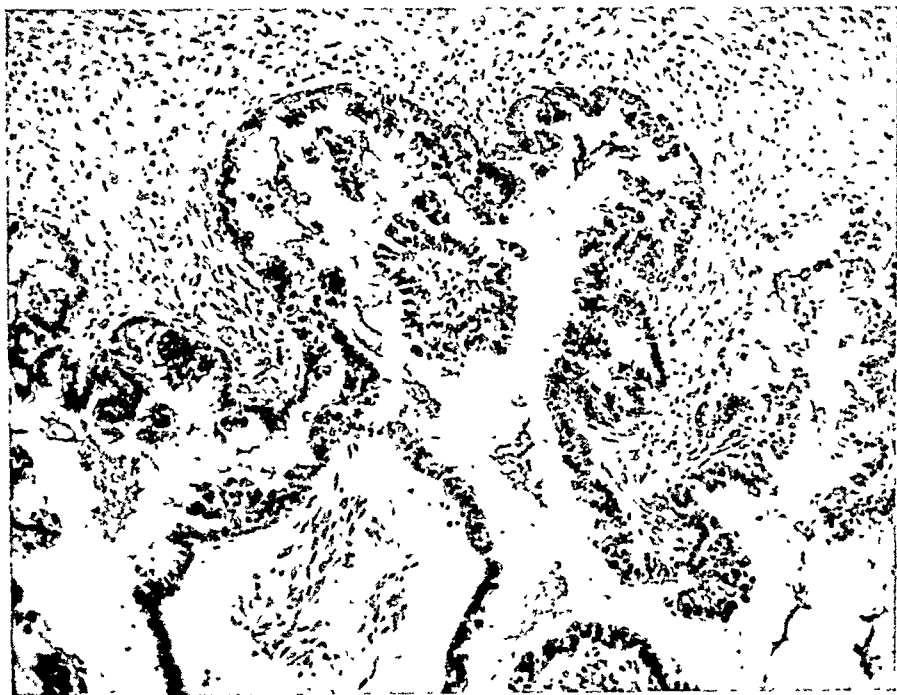


Fig. 2.—Sloane Hospital Pathology No. 6920 (Mrs. E. S.) shows microscopic appearance of ovarian tumor tissue after radiation.

Microscopic Examination: (Fig. 2.) The uterus was not remarkable except for the presence of an endometrial mucous polyp. In the serosa of both tubes, dilated lymph channels were seen which contained epithelial cells resembling the epithelium of the tumor masses. On the outer wall of the cyst were a number of papillary excrescences covered with tall atypical columnar epithelium. The nuclei varied in size, shape and staining quality. Some mitotic figures were seen. In some areas the basement membrane was absent and the underlying stroma was invaded by tumor cells. There were a few small masses of bluish-staining calcified material in several areas in the cyst wall. The epithelium lining the cyst was similar to that described on the outer wall.

Diagnosis: Endometrial polyp; atrophy of endometrium; atrophy of uterus,
The right tube showing lymphatic extension of growth,
Papillary cystadenocarcinoma, right ovary,
Left tube showing lymphatic extension of growth, and
Papillary cystadenocarcinoma, left ovary.

This patient had an uneventful convalescence and has remained well. The abdominal wall was firm and the pelvis was clear. It has now been eleven years after the first operation, and ten years since the second operation, and she was last seen in the Follow-up Tumor Clinic on October 8, 1943.

CASE 2.—Mrs. L., Unit No. 485440, a thirty-year-old married nulligravida, was admitted to the Presbyterian Hospital on April 24, 1936, with a history of having had fever and night sweats for six weeks. During most of this time, the abdomen was distended. For the past two weeks, she had had abdominal cramps. A diagnosis of tuberculous peritonitis or possibly an ovarian cyst was made, and on May 7, 1936, an exploratory celiotomy was done.

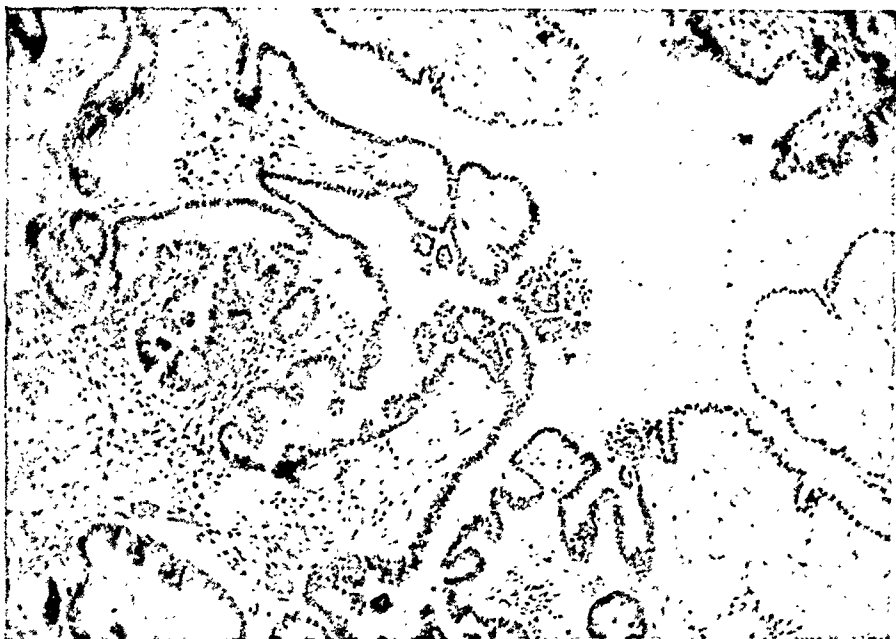


Fig. 3.—Presbyterian Hospital Pathology No. 60732 (Mrs. L.) shows microscopic appearance of ovarian tumor removed at primary operation before radiation.

The abdomen contained approximately 12 liters of straw-colored fluid. The upper abdomen seemed to be normal. The liver was smooth, the kidneys were of normal size and also the spleen. The small bowel was injected, but otherwise was normal. The pelvis was filled by a dense matted mass of adhesions and the individual structures could not be identified. Just beneath the bladder was a shelf of grayish-fibrinous tissue, which seemed to form a bridge across the pelvis and through this passed the sigmoid. The appendix was edematous and adherent to the shelf of tissue. Deep in the pelvis was a considerable quantity of friable grayish-white material resembling the implantations occurring with papillary carcinoma of the ovary. "Because it was apparent that nothing surgical could be done, we were satisfied with removing some pieces of this tissue for pathological examination and proceeded to close the wound."

Microscopic Examination: (Fig. 3.) The specimen was quite glandular. Cells varied in size and shape and staining quality, with vesicular nuclei which showed about three mitotic figures per high power field. The tumor was thought to be anaplastic.

Pathological Diagnosis: Papillary carcinoma of the ovary.

The postoperative course was uneventful and the patient left the hospital on the twenty-third day. The wound healed by primary union. Deep x-ray therapy was begun on the sixth postoperative day and apparently caused some nausea. Between May 13, and May 29, 1936, when the patient was discharged, fifteen exposures of deep x-ray were given to the pelvic region, through three fields, two anterior and one posterior, each measuring 10 cm. by 15 centimeters.

Each exposure was as follows: Kilovolts, 200, Anode skin distance, 50 cm., Filter, 1.0 mm. copper and 1.0 mm. aluminum, Total 1,050 r. for each anterior field and 150 r. for the posterior field.

This series was completed at the Queens General Hospital between June 4, and June 23, 1936: 1,050 r. were given to the posterior right and posterior left pelvis, 150 r. were given daily filtered with $\frac{1}{2}$ mm. of copper and 1.0 mm. aluminum. On admission to the Roentgenological Department of the Queens General Hospital, the patient appeared to be debilitated, and the entire pelvis was thought to be filled with a firm diffuse nontender mass. On June 21, 1936, the following notation was made, "Patient is now greatly improved. Her appetite is good. The ascites has entirely cleared. On vaginal examination, the pelvic mass was found to be considerably smaller and softer."



Fig. 4.—Sloane Hospital Pathology No. 10802 (Mrs. L.) shows microscopic appearance of ovarian tumor tissue after radiation.

On December 8, 1936, a laparotomy was performed at Sloane Hospital for Women. A moderate amount of clear fluid was present in the abdominal cavity. On both sides, in the region of the ovaries, were cystic masses of friable tissue approximately 8 cm. in diameter, which were adherent to the side wall of the pelvis and to the intestines, but did not involve the peritoneum, omentum or any other structures. Both tubes and ovaries were removed. The uterus was not removed.

Microscopic Examination: (Fig. 4.) Irregular papillary excrescences and partially hyalinized fibrous tissue suggestive of psammoma bodies were seen. The projections were covered for the most part with a single layer of columnar epithelium. In some areas, however, the cells were found to be grouped in several layers giving the appearance of pseudostratification. There was relatively little change in the size, shape and staining quality of the cells. Occasional mitotic figures were observed.

A diagnosis of papillary cystadenoma was made.

Convalescence was uneventful and the patient weighed 103½ pounds when discharged from the hospital. Stilbestrol was given for hot flushes. She attends the Tumor Clinic at regular intervals and when last seen on January 7, 1944, her weight was 138½ pounds, her general condition was good and her pelvis was clear. It has now been seven and one-half years since her first operation, and seven years since her second operation.

CASE 3.—Mrs. I. G. P., Unit No. 429174. A thirty-one-year-old nullipara was admitted to Sloan Hospital for Women because of abdominal swelling and discomfort of one month's duration. A diagnosis of tuberculous peritonitis or ovarian neoplasm was made, and on January 25, 1934, a laparotomy was done. A large amount of ascitic fluid was found, the peritoneum was injected and adhesions were present between the pelvic mass and the intestines. The pelvis was filled with a pinkish-white cauliflower growth which extended to the level of the umbilicus. It was felt that excision was not feasible and a biopsy was taken. Microscopic study showed that the tumor was a malignant papillary serous cystadenoma of the ovary. (Fig. 5.)



Fig. 5.—Sloane Hospital Pathology No. 8396 (Mrs. I. G. P.) shows microscopic appearance of ovarian tumor tissue before radiation.

On January 10, 1936, the patient was seen in the Tumor Follow-up Clinic. She was in a debilitated condition and had had numerous paracenteses for recurring ascites. She was remarkably free from symptoms except for abdominal discomfort due to tension when a paracentesis was needed. The abdominal mass was unchanged. In view of our experience with the two previous cases, it was decided to try x-ray therapy.

Between January 15, 1936 and July 8, 1936, fifty-eight exposures of deep x-ray were given, through four fields, two anterior and two posterior, each measuring 15 cm. by 15 centimeters.

Each exposure was as follows: Kilovolts, 190 to 200, anode skin distance 50 cm., filter 0.55 mm. copper and 1.0 mm. aluminum, total 1,600 r. for each of the anterior fields, and 1,000 r. for each of the posterior fields.

Following roentgen therapy, the abdominal mass was reduced in size. Improvement was noted in the patient's general condition, and there was less localized pain.

A second laparotomy was planned with the possibility of removing the pelvic growths. On December 11, 1936, the operation was per-

formed and large masses of glistening white cauliflower-like tissue were found extending halfway to the umbilicus. The tissue was soft and friable. The liver was smooth. A hysterectomy and bilateral salpingo-oophorectomy were performed and the diagnosis of carcinoma of the ovary was confirmed microscopically. (Fig. 6.) The operation was complicated by peritoneal adhesions which were probably due, at least in part, to the 85 paracenteses that were done in the two years prior to the operation.



Fig. 6.—Sloane Hospital Pathology No. 10812 (Mrs. I. G. P.) shows microscopic appearance of ovarian tumor tissue after radiation.

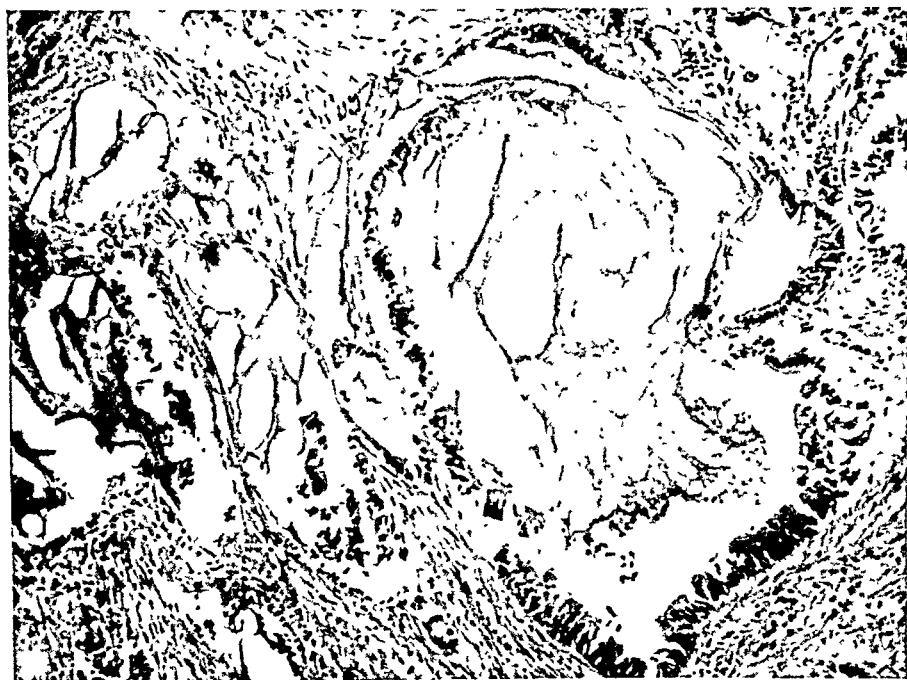


Fig. 7.—Presbyterian Hospital Autopsy No. 13028 (Mrs. I. G. P.) shows microscopic appearance of tumor of the intestine which resulted in perforation and death of the patient.

The postoperative course was satisfactory and the patient left the hospital on the sixteenth day. General improvement was noted and examination showed the abdomen firm and the pelvis clear. She resumed a normal life, came to the Follow-up Clinic at regular intervals, and did some work as a substitute public schoolteacher. In February,

1939, she was admitted as an emergency after a two weeks' illness, a diagnosis of intestinal obstruction was made and a cecostomy was done on February 27, 1939. The patient died shortly after the operation. Autopsy revealed no evidence of carcinoma of the ovary. The cause of death was perforated carcinoma of the colon.

Autopsy (No. 13028).—A. M. Pappenheimer: "Quite unexpectedly there was disclosed at autopsy a perforated adenocarcinoma of the sigmoid, located several inches above the site of the previous pelvic tumors; there was one small metastatic nodule in the pelvic tissue, but no distant metastases. The histological structure of the tumor of the colon (Fig. 7) is that of a colloid adenocarcinoma, which is unquestionably unrelated to the ovarian tumor. The regression of her ovarian tumors is complete, save in one portion of the remaining ovarian tissue in which there are still found a few papillary cysts lined by low, not actively growing epithelium, which may represent the remains of the original growth. There is not a trace of the previous peritoneal implantations. The case is instructive in demonstrating the possibility of curing what was probably a malignant epithelial tumor, and in showing that the regression of one epithelial neoplasm confers no immunity to the development of a new spontaneous carcinoma."

Discussion

The most interesting point in these cases is the clinical experience in three cases suffering with apparently inoperable ovarian tumors which were made operable by x-ray therapy.

Should these cases be called carcinoma? Grossly, they were definitely malignant. There was massive local extension to the pelvic wall and intestine and infiltration preventing separation of the growth from the surrounding structures and peritoneal implants. As in many ovarian neoplasms, the process was limited to the abdominal cavity. Microscopically, the evidence of malignancy was unsatisfactory as in most of the papillary growths of the ovary. Morphologically, there was only occasional evidence of rupture of the basal membrane and infiltration. Cytologically, there was some variation in the size and shape of the cells, some loss of polarity of the nucleus and slight increase in mitoses. On the whole, however, it would be impossible to classify any of the three neoplasms as definitely benign or definitely malignant.

The effects of the radiation are similarly apparent in gross rather than in microscopic changes. The size of the mass was reduced. It became localized. The most striking effect was the elimination of infiltration. This permitted the papillary process which still persisted to be separated easily from intestines and the parietal peritoneum. Isolated peritoneal implants also disappeared. Microscopically, there was a slight flattening of the cells and a return of the nuclei to the base of the cells.

Summary

1. Three cases of papillary cystadenocarcinoma, inoperable because of massive infiltration into the surrounding structures, are presented which were apparently made operable by deep x-ray therapy.

2. In all three cases the neoplasm was limited to the abdominal cavity.

3. The x-ray profoundly affected the gross appearance of the tumors, but caused very little change in the microscopic picture.

4. Two of the patients are alive after eight and twelve years, respectively; the third succumbed after five years of an apparently unrelated carcinoma.

Conclusions

1. Deep x-ray therapy in the three cases reported caused the papillary excrescences and transplants to shrink and the entire mass to diminish in size, thus making operation easier.

2. This study indicates that it is unwise to persist in doing a difficult primary operation. In some cases of massive infiltration, it may be safer to take a biopsy, close the abdomen, give deep x-ray and perform a second operation at a later time.

References

1. Ford, F. A.: *AM. J. OBST. & GYNEC.* 16: 1, 1928.
2. Montgomery, J. B., and Farrell, J. T. Jr.: *Radiology* 23: 157, 1934.
3. Kean, A.: *Am. J. Surg.* 27: 425, 1935.
4. Taylor, H. C. Jr., and Greely, A. V.: *Surg., Gynec. & Obst.* 74: 928, 1942.
5. Schmitz, H. E.: *West. J. Surg.* 50: 445, 1942.
6. Harris, J. H., and Payne, F. L.: *AM. J. OBST. & GYNEC.* 29: 88, 1935.
7. Lynch, F. W.: *AM. J. OBST. & GYNEC.* 32: 753, 1936.
8. Meigs, J. V.: *Surg., Gynec. & Obst.* 71: 44, 1940.
9. Goodall, J. R.: *AM. J. OBST. & GYNEC.* 43: 210, 1942.
10. Geist, S. H.: *Ovarian Tumors*, New York and London, 1942, Paul B. Hoeber, Inc., p. 202.
11. Marchetti, A. A.: *New York State J. Med.* 41: 2324, 1941.

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Discussion

DR. JAMES A. CORSCADEN.—I observed the original condition of two of the cases and all three at the secondary operation. Most dramatic was the change in the gross appearance. In all three cases the growth infiltrated the surrounding tissues, the pelvic wall and intestines. At the second operation, there were still masses of cauliflower tissue but they could be separated cleanly from the surrounding tissue.

The second point which interests me is the contrast between the gross appearance of these growths and the microscopic picture, one having every aspect of malignancy, the other showing few of the characteristics of an invasive carcinoma.

The practical application of the experience in these three cases would be that, in apparently hopeless, invasive cases, to carry out the procedure performed here,—the exploratory incision, the taking only of a biopsy and no attempt made to scoop out the removable material, the giving of adequate x-ray therapy and a second operation several months later. Certainly the partial removal of ovarian carcinoma and subsequent radiation has not given very satisfactory results. The other procedure would at least be worth trying.

GANGRENE OF AN EXTREMITY IN A NEWBORN CHILD

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THE following instance of gangrene of an extremity in a newborn infant is recorded in order to draw attention to an apparently rare fetal condition, of which, to date, only 42 cases seem to have been reported in the literature.

Case Report

A white multipara, 33 years of age, was first seen at the Hutchinson Memorial Clinic of the Tulane University of Louisiana School of Medicine April 13, 1938, in the tenth week of her eighth pregnancy. The last menstrual period had occurred February 7, and the estimated date of confinement was November 14, 1938.

The patient's seven previous pregnancies had been without incident and had terminated in spontaneous full-term deliveries. Inquiry into the personal and family history revealed nothing of significance. Physical examination revealed no abnormalities and the pelvic measurements were adequate. The blood serologic reaction was negative and all other laboratory data were within the normal range of values.

The pregnancy progressed uneventfully. Fetal movements were felt early in July. The initial blood pressure was 115/80 and the highest pressure, 130/90, was observed September 22. The patient weighed 147 pounds on her first visit to the clinic, and 177 pounds October 11, 1938.

The following day the membranes ruptured and a large amount of water was lost. No pelvic examination was made at this time. When labor had not ensued at the end of 48 hours, medical induction was carried out by the use of castor oil followed by a hot enema. Pains occurred promptly, and pelvic examination an hour later showed the cervix fully dilated and entirely effaced. The presentation was vertex and the position L.O.A. The fetal heart tones were strong. After a 20-minute second stage a viable male child, weighing 10 pounds, was delivered spontaneously and without difficulty, except that as the head was delivered, the left hand was found to be prolapsed between the cranium and the bony pelvis.

The child cried promptly and was normal in all respects except that the skin was missing from, and a wide path of excoriation involving, the dorsal surface of the first phalanges of the second, third, fourth and fifth fingers. The remainder of the hand presented a normal pinkish hue and arterial pulsations in the extremity were of normal strength. The entire extremity, however, seemed incapable of active motion.

As the day progressed the child's respirations became rather shallow and the hand began to assume a bluish-red tinge. Sixteen hours after birth he was admitted to Touro Infirmary, at which time the following notes were made:

This is a full-term newborn male child, whose physical findings present no abnormalities except as follows:

The face is very red and slightly edematous. Respiration is rapid and shallow and inspiration is occasionally accompanied by a moan or grunt. There is dullness over a small area posteriorly at the level of the angle of the scapula, and subcrepitant râles are heard over the same area. The left arm lies limply by the baby's side; passive motion causes pain, and active motion seems impossible. The forearm and hand are slightly edematous. Across the dorsum of the first phalanx of the second, third, fourth and fifth fingers is a bright red excoriation about 1 cm. wide. The fingers and fingernails are blue, the color being deepest on the second and fourth fingers. A purplish discoloration extends up the thumb

to the dorsum of the hand. Arterial pulsations are of normal strength. The whole extremity feels rather cool.

Spinal puncture revealed clear fluid under no increase in pressure. Examination of the fluid showed 30 white blood cells and many red blood cells per high power field. The globulin content was within normal range.

The child was assumed to have pneumonia and was placed on the routine pneumonia regimen, including the oxygen tent. Within 24 hours the lung findings were normal and it was concluded that they were due to pulmonary congestion rather than to pneumonia.

A surgical consultant believed that the condition of the left hand was caused by ecchymosis rather than by incipient gangrene, and advised conservative therapy, including heat and elevation of the extremity. For 48 hours slight improvement seemed to be occurring. The fingers remained dark and cool, but the extremity became warmer elsewhere, and the swelling disappeared. At the end of this period, however, definite progression occurred, and by the tenth day of life the distal two-thirds of all the digits, including the thumb, were clearly gangrenous and an irregular line of demarcation could be traced on the dorsum of the hand at the base of the fingers and on the volar aspect about the middle of the palm. The whole extremity was cold and arterial pulsations could not be felt.

Amputation of the forearm was carried out the following day, under drop ether anesthesia. A guillotine amputation just above the left wrist was attended with practically no bleeding, and reamputation was therefore done at the junction of the upper and middle third of the forearm, at which level the blood supply seemed entirely normal.

The pathologist reported as follows:

One specimen consists of an infant's left hand and 5 cm. of the distal portion of the forearm. All five fingers are involved in a gangrenous process which terminates grossly at the metacarpophalangeal articulation. There is some loss of skin over the palmar surface of the hand. The tissue is degenerated and gangrenous, and some of the blood vessels are distended, but definite thrombosis or other abnormalities cannot be demonstrated in any of the areas examined.

The other specimen, which consists of a portion of forearm, presents no abnormalities.

The child was not disturbed by the operation and continued to nourish well and gain weight. A rather extensive slough and wound infection in the stump required the removal of the sutures (interrupted dermal) on the fifth day, and the use of various local measures as well as injections of whole blood and ultraviolet therapy. The soft tissues of the axilla and about the shoulder joint were involved in an infectious myositis before the process was brought under control, but the child was in excellent condition and the wound was well healed when he was discharged from the hospital on the thirty-fourth postoperative day. At this time he had full motion of the stump.

Examination at the age of seven weeks in the Pediatrics Clinic of the Tulane University Hutchinson Memorial Clinic showed no abnormality except the absence of the upper left extremity. The gain in weight had been average for the duration of life. The blood serologic reaction was negative, and values for all blood elements were within normal range. The mother was carefully questioned at this time concerning possible abnormalities of pregnancy or parturition on either side of the family, but none was revealed.

The child continued to gain normally until the age of three months, at which time he developed bronchopneumonia, which proved fatal. Autopsy was not permitted.

Discussion

Gangrene of an extremity in the newborn infant is an apparently very rare occurrence. According to Heller and Alv¹ who made a

complete review of the literature and a tabulation of reported cases in 1941, there had been recorded to date 40 cases, including their own, of which nine, including their own, were instances of gangrene of the upper extremity, and of which five, including their own, were reported in the American literature. Their comprehensive study supplements Kosmak's² report in 1908, of one personal and four collected cases, and Dohan's³ report in 1934, of one personal and 25 reported cases.

Kosmak omitted several cases which Dohan and Heller and Alvari included in their later reviews. The latter authors, however, omitted Bronson's case, reported in the *Transactions of the American Dermatological Association* in 1901, and included in Dohan's report; in this instance the gangrene involved the right cheek, neck, ear, clavicle and thumb. Durand and Bobillo⁴ have since reported (1935), a case of symmetrical gangrene of the lower extremities and superficial gangrene of the left forearm. The inclusion of these two cases and the addition of the case reported herewith bring to 43 the number of recorded cases, to 12 the number of cases of gangrene of the upper extremities, and to 7 the number of cases recorded in the American literature. It might be added that an examination of the literature, since 1941, has revealed only one possible additional case. It is in a German publication which is not available to me, and the title is not sufficiently specific to permit a definite statement that the case is one of gangrene of the newborn infant.

In addition to the 7 cases recorded to date in the American literature, 4 others have been reported in the English, and 1 in the Australian literature. No reasonable explanation presents itself for the preponderance of reports in the foreign literature. As in all "rare" conditions, undoubtedly many cases have occurred which have not been reported, but there also seems no doubt that gangrene of the newborn infant is actually very rare. The subject is not mentioned in textbooks of obstetrics, and 11 leading obstetricians in the United States who were questioned concerning it replied that they had never observed it or even heard of it, though all of them had had personal experience with compound presentations.

The only case in any way similar to my own and the other reported cases observed by any member of this group was described by Dr. J. W. Harris:⁵ A child delivered after a prolonged dry labor presented just above the knee a spiral depression completely encircling the thigh, into which the umbilical cord fitted with ease. Below the depression the leg was enormously edematous, cold, and almost black. Gangrene seemed inevitable, but recovery ensued under conservative therapy. The condition was explained as due to interference with the circulation by the umbilical cord which encircled the thigh.

In the 43 cases reported to date, the outcome is in doubt in 5 instances, and 16 children are known to have died of the condition. Deferred death occurred in my own case, but it is highly doubtful that the gangrene had any part in the fatality.

The most baffling feature of gangrene of the newborn infant is the etiologic factor. In certain of the reported cases the suggested causes are unconvincing. In Cotes-Predy's⁶ case, for instance, maternal trauma is advanced as the cause of fatal fetal gangrene, the mother having fallen on the right side twice before delivery. The evidence advanced for the diabetic etiology suggested in Lawrence and McCance's⁷ case is of dubious worth, and Raynaud's disease, suggested as a cause in 4 reported cases, is unlikely in newborn infants, for obvious reasons. Infection was a reasonable possibility in some though not in all of the cases in which it was suggested.

The most logical cause suggested in the reported cases was trauma at delivery. As Heller and Alvari point out, the incidence of hard, difficult labor, abnormal delivery and neonatal asphyxia in the 40 cases they collected is far above the proportion to be expected in so small a series. In the 39 cases in which details were available, labor

was difficult or birth instrumental or otherwise abnormal in 11 instances, the cord was about the child's neck in two instances, and the baby was asphyxiated, or otherwise abnormal in 8 instances.

It is interesting that the majority of obstetricians who were questioned on the subject, as previously mentioned, advanced trauma at delivery as the most reasonable explanation. Bayard Carter,⁸ for instance, reasoned that if pressure necrosis of the scalp can occur, it seems logical that pressure on the prolapsed extremity in a compound presentation can produce the same result. A. C. Beck⁹ stated that he always discusses pressure necrosis as a theoretical possibility in prolonged labors with prolapse of the hand when he is lecturing to students. In his opinion gangrene would occur more often except for two circumstances, that many cases are promptly recognized and treated either by replacement of the hand or by version, and that there is a high percentage of stillbirths in such cases.

In my own case, there seems little doubt that the gangrene can be attributed to prolonged pressure on the prolapsed hand caught between the head and the bony pelvis. It can reasonably be assumed (though no pelvic examination was made at the time), that the hand prolapsed at the time the membranes ruptured and that the pressure was continuous until delivery 50 hours later. A somewhat similar case was reported by Fischer¹⁰ in 1929: The midwife who attended an 18-year-old primipara stated that after 14½ hours of hard labor, the child was born with the palm of the right hand over the right eye, and with the umbilical cord around the neck. Gangrene was apparent a week after birth, but the child was not seen until the eleventh day; his condition then did not permit amputation and death occurred on the fourteenth day. Postmortem examination showed thrombus-formation in the great vessels of the right arm, pulmonary arteries and aorta. In my own case, pathologic examination of the amputated extremity failed to show thrombus-formation.

In my own case, there was ample amniotic fluid, and amniotic adhesions could not have caused the gangrene. It is unlikely that it was due to focal deficiencies, as studied by Streeter,¹¹ for in such cases, as he pointed out, "the defect usually is present in some degree in all four extremities, and at least in two or more."

Heller and Alvari have outlined a plausible and ingenious mechanism to explain the gangrene in their personal case. Delivery was by midforceps, resorted to after 29 hours of hard labor because of maternal exhaustion. The child was in poor condition at birth and presented cyanosis and asphyxia. The following day the right arm was found to be paralyzed and the right hand was cold, limp and blue. Two days later a gangrenous process involved practically the whole right upper extremity below the elbow, and pulsation could not be detected in either the axillary or radial artery. Amputation was considered and decided against, and conservative treatment was instituted, with ultimate preservation of the extremity and with only limited loss of function.

These authors do not believe that if true thrombus-formation had been present, canalization could have been established in so short a time. They also point out that freeing of a thrombus would have resulted in a more dramatic episode distal to the axillary artery than that which occurred, and that rapid establishment of collateral circulation need not be assumed, because the axillary artery resumed pulsation six days after birth.

Their hypothesis is that "there existed a temporary agglutination of the intimal surfaces of the large vessel . . . similar to that which occurs when a piece of rubber tubing of equivalent caliber is pressed on firmly for a protracted period. Perhaps the surfaces were sealed with fibrin, which essentially shut off all distal supply of blood but was not necessarily accompanied by thrombus-formation. When the pressure was no longer a factor, the proximal pulsating blood stream,

acted as a hydrostatic wedge, and the adhered surfaces gradually were forced apart and circulation again established soon enough to preserve function but not before a modicum of damage had been done."

This hypothesis seems more generally applicable than any other which has been suggested. It is particularly applicable to the cases of gangrene of the extremity in which recovery occurred under conservative treatment, and it is also applicable to the cases in which amputation was necessary or in which no surgery was practiced and death occurred. In such cases, as in my own, the pressure may have lasted too long to permit separation of the adhered surfaces after it was relieved.

Heller and Alvari, on the basis of this hypothesis, suggest that in the absence of gross infection, a mutilating procedure should be postponed until it is certain that it cannot be avoided. The advice, of course, is sound, for amputation of an extremity is a repugnant operation at any age, and particularly repugnant in a newborn baby. On the other hand, it sometimes cannot be avoided. In Heller and Alvari's case, pulsation in the axillary artery was felt on the sixth day and pulsation of the radial pulse on the twelfth day, but in my own case these pulsations, originally present, disappeared under conservative therapy and the gangrenous process continued to spread. The warning should also be uttered that in one's natural desire to be conservative, radical surgery should not be delayed too long, as it apparently was in some instances in the reported series in which death occurred without operation.

Diagnosis is usually clear-cut. In my own case, as in Heller and Alvari's case and in one of the cases reported by Lévy,¹² limitation of motion, which in my own case and in Heller and Alvari's case amounted to actual paralysis, was antecedent to the gangrenous process, and in such cases, as Lévy notes, Parrot's pseudoparalysis must be differentiated.

The practical importance of this case report is, as E. D. Plass¹³ points out, the recognition of "a new danger from premature rupture of the membranes." It is the practice of many obstetricians in such instances to avoid pelvic examination until after pains have begun and labor has progressed, and that practice was followed in this instance. It may be that under such circumstances immediate pelvic examination might be the wiser plan.

Summary

A case is reported of gangrene of the upper left extremity in a newborn infant, born 50 hours after rupture of the membranes and two hours after the onset of labor; at delivery the affected extremity was found prolapsed between the cranium and the bony pelvis. Conservative therapy was ineffective and amputation was necessary on the eleventh day of life.

To date, 42 similar cases have been reported in the literature, of which 11 were instances of gangrene of the upper extremity.

The etiology is briefly discussed, and trauma is shown to be the most reasonable and most generally applicable cause of the condition.

References

1. Heller, George, and Alvari, George: *Am. J. Dis. Child.* 62: 133, 1941.
2. Kosmak, G. W.: *Bull. Lying-in Hosp.* 4: 124, 1908.
3. Dohan, F. C.: *J. Pediat.* 5: 756, 1934.
4. Durand, C. M., and Bobillo, I. D.: *Semana méd.* 2: 725, 1935.
5. Harris, J. W.: Personal communication.
6. Cotes-Preedy, D.: *Lancet* 1: 575, 1904.
7. Lawrence, R. D., and McCance, R. A.: *Arch. Dis. Childhood* 6: 343, 1941.
8. Carter, Bayard: Personal communication.
9. Beck, A. C.: Personal communication.
10. Fischer, W.: Cited by Heller and Alvari.
11. Streeter, G. L.: Personal communication.
12. Lévy, Georges: *Monde méd. Paris* 49: 542, 1939.
13. Plass, E. D.: Personal communication.

ADENOACANTHOMA OF THE OVARY

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THE term adenoacanthoma is applied to tumors composed of glandular and squamous elements;¹ these neoplasms are sometimes known as adenocanceroids. Descriptions of such lesions encountered in the esophagus, stomach, gall bladder, pancreas, sigmoid, thyroid, and lung have been reported sporadically in the literature. The fact that occasionally, carcinomas of the corpus uteri are composed of both glandular and squamous cells is well known. Among 100 cases of carcinoma of the body of the uterus, Healy and Cutler² found 3 adenoacanthomas. Lindsay,³ in 1927, reported 3 instances of adenoacanthoma in a series of 70 cases of corpus carcinoma. The occurrence of metastatic adenoacanthoma of the ovary from a primary adenoacanthoma in the body of the uterus is mentioned by Meigs.⁴ The authors have been unable to find a single instance of primary adenoacanthoma of the ovary in the literature at their disposal. Inasmuch as two patients, who presented such a neoplasm, were encountered recently on the gynecology service of University Hospitals, it is felt that the reporting of such an unusual lesion would be in order.

Case Reports

CASE 1.—(History No. 225-530; Pathology No. 74739.) This was a 69-year-old white housewife, who was admitted to the gynecology service of University Hospitals with a complaint of vaginal bleeding for one month. The bleeding had been intermittent, and there had been no clots; no pain; no weight loss. The patient gave a history of having had scarlet and typhoid fevers. There had been two normal pregnancies; no abortions. Review of systems was not revealing. The menses began at the age of 13 years, and occurred regularly every 28 days lasting for 7 days. The last menstrual period was 26 years previously. Physical examination revealed a healthy appearing elderly white woman, in no particular distress. The findings on general physical examination were entirely within normal limits. Pelvic examination, however, disclosed a relaxed vaginal outlet; cervix anterior and atrophic; fundus uteri forward and apparently normal. Both adnexal regions were occupied by firm, nodular tumor masses. On laboratory examination, the urinary findings and blood count were within normal limits. Radiogram of chest showed no evidence of parenchymal infiltration in the lung fields.

On November 23, 1942, pelvic laparotomy was carried out under gas-oxygen-ether anesthesia. The left ovary was nodular and cystic, and measured 14 cm. in greatest diameter. The ovarian mass was adherent to the broad ligament anteriorly, and the left Fallopian tube was drawn out over its superior surface. The corpus uteri was entirely normal in size, color, and consistency. The right ovary, however, was the size of a man's fist, and was white and glistening in appearance; it was nowhere adherent. Bilateral oophorectomy and left salpingectomy were carried out; however, because of the patient's unsatisfactory condition under anesthesia, hysterectomy was not undertaken. Following operation, the patient made a satisfactory convalescence, and was discharged from the hospital on the twenty-first postoperative day. Despite the exhortation of the staff, the patient refused to undergo diagnostic curettage before going home. This procedure was urged so that the absence of

corpus cancer could be definitely established, despite the fact that there was no clinical evidence of such a lesion.

Pathologic Examination.—The (left) ovary weighs 735 Gm., and measures 14 by 11 by 6.5 centimeters. The external surface is relatively smooth. Occasional daughter cysts varying from 2.5 by 2 to 6 by 4 cm. contain light-brown, glairy material. The ovary is essentially a sac, and varies from 0.5 to 1 mm. in thickness. Sections taken through the cystic portions show the cystic spaces to vary considerably in size. They are all lined with columnar epithelium that in most instances is a single layer in thickness. These cells are fairly uniform in type and many are ciliated. Sections from other portions of the ovary show tumor which is pleomorphic and of epithelial type. Throughout there are papillae with slender connective tissue cores, that are covered with columnar epithelium. There are numerous glands that vary considerably in size. The glands are lined with columnar epithelial cells. Some of these cells have atypical irregularly shaped hyperchromatic nuclei and others have mitotic figures, some of which are abnormal. In addition throughout, there are groups of cells that are definitely of squamous type. In some regions there is considerable keratohyaline material. The tumor is definitely invasive, there being identifiable glands lined by tumor cells situated in the ovarian stroma.



Fig. 1.—Case 1. Adenoacanthoma of the ovary. Photomicrograph ($\times 120$) showing large plaques of squamous epithelium, containing abundant keratohyaline material. Sections from Case 2 are strikingly similar to those from Case 1, except for slightly less squamatization.

The tube measures 12 by 0.6 centimeters. It is smooth reddish gray, and the fimbriated end is occluded and adherent to the ovary. The lumen is patent, empty, and is not dilated. The wall is not unusually thickened. Sections of the uterine tube show the lumen to be patent. The plicae are unusually large, and some are club-shaped. They are covered with simple columnar epithelium. There is no significant cellular infiltration in the sections examined.

The (right ovarian) tumor mass weighs 180 grams and measures 9 by 6 by 5 centimeters. The external surface is unusually smooth and light-pinkish gray. The cut surface neither bulges nor retracts, and is pearly gray. There is no obvious degenerative change. Sections show the tumor mass to be richly cellular and definitely edematous. The cells

vary in size and shape; some are elongated and spindle in outline. These have acidophilic cytoplasm. Others are somewhat stellate in type, and some are oval. They have relatively large nuclei, many of which are irregularly shaped and deeply chromatic. There are no bizarre nuclear forms, or abnormal mitotic figures. The tissue separating these cells is loosely arranged, of connective tissue type, and is distinctly edematous.

Diagnosis:

1. Papilliferous serous cystadenocarcinoma of ovary, showing marked squamous metaplasia.
2. Fibroma of other ovary.
3. Healed salpingitis.

Since operation (November 23, 1942), the patient has been entirely asymptomatic: there has been no abdominal pain; no vaginal discharge or bleeding; and, no loss of weight. Vaginal examination at this time (August 28, 1944) reveals an atrophic uterus, and entirely negative adnexa. Thorough uterine curettage was done on August 28, 1944, but hardly any tissue was obtained. The pathologic report on the surgical specimen was "material insufficient for diagnosis."

CASE 2.—(History No. 235-207; Pathology No. 83273.) This was a 61-year-old colored cook, who was admitted to the gynecology service of University Hospitals on April 24, 1944. The patient's chief complaint was lower abdominal swelling for three months. The patient stated that during the course of her illness, there had been a gradually enlarging tumor in the lower left abdomen. Aside from the tumor, the only other symptom had been recurrent bouts of lower abdominal pain. The patient gave a history of a pelvic laparotomy, in which the right ovary is alleged to have been removed, 30 years previously in another state. Past history included but one pregnancy, which was said to have terminated in early abortion. In 1934, duodenal ulcer was diagnosed at this hospital. Menopause occurred in 1927, since which time there has been no vaginal bleeding.

At the time of admission to the hospital, the patient appeared normally developed and well nourished. General physical examination disclosed the heart to be somewhat enlarged to the left and a systolic murmur could be heard over the base of the heart. Blood pressure was 160/110 mm. mercury. On abdominal examination, a remote lower midline surgical scar was seen. An obvious mass occupied the entire lower left abdominal quadrant. The tumor was tensely fluctuant in consistency, and not especially tender. Liver, spleen and kidneys were not palpated, and there was no evidence of free abdominal fluid. On pelvic examination, the outlet was marital, but well supported. The cervix was clean and anterior. The corpus uteri was taken to be about normal in size, and could be palpated separately from the tumor mass in the left adnexal region. The mass was fluctuant but not tender. Nothing abnormal was made out in the right adnexal region. Results of urinalysis were negative. Erythrocytes numbered 4,000,000 and the value for hemoglobin was 67 per cent (Sahli). Results of the serologic test for syphilis were negative.

On April 25, 1944, pelvic laparotomy was carried out with the patient under the influence of gas-oxygen-ether anesthesia. Lysis of adhesions, subtotal hysterectomy and left oophorocystectomy were performed. The mass described above proved to be a left ovarian cyst; it was adherent to loops of small bowel in several places, and adherent to the sigmoid and posterior surface of the uterus. The right adnexal structures were found to be missing from a previous operation. The patient withstood the operative procedure fairly well, and was returned to bed in satisfactory condition. The postoperative course was interrupted by mechanical bowel obstruction, which required laparotomy and the lysis of

adhesions on the fifteenth postoperative day. Subsequently, the patient developed pleurisy with encapsulated effusion, which gradually resorbed. However, the patient was discharged from the hospital in satisfactory condition on the fortieth hospital day.

Pathologic Examination.—The ovarian tumor measured 13.5 cm., and grossly showed a striking resemblance to the carcinoma removed in Case 1. Microscopically, sections of the ovary show the tumor to be of epithelial glandular type. The glands are lined with high columnar epithelium and vary greatly in size. Irregularly shaped hyperchromatic nuclei render many of the epithelial cells atypical. Some of the mitoses are abnormal. There is a focal distribution of identifiable acidophilic keratohyaline material. Extensive necrosis and infiltration with neutrophilic polymorphonuclear leucocytes may be seen in some fields. Grossly, the uterus is atrophic; it weighs 30 grams, and measures 5.0 by 4.0 by 1.5 centimeters. Scattered through the myometrium are three firm encapsulated tumors, from 5 to 12 mm. in diameter. On section, these tumors have a bulging, white, whorled cut surface. The endometrium is intact, and is thin pinkish-white in color. The serosa is shiny and transparent.

Diagnosis:

1. Partially differentiated cystadenocarcinoma of ovary with focal squamous metaplasia, acute inflammation and necrosis.
2. Fibromyomas and atrophy of uterus.

Discussion

The histogenesis of adenosquamous carcinoma is a moot question. A voluminous literature has been written on the subject of adenoacanthoma of the body of the uterus. It is the conclusion of Novak⁵ that the "epidermization" seen in fundal adenoacanthoma is the result of metaplasia of the cylindrical to the squamous type of epithelium. A study of cervical biopsy material reveals the very great frequency of metaplasia of the normal columnar to the squamous type of epithelium, in inflammatory lesions of the cervix uteri. Moreover, it is recognized that the germinal epithelium covering ovaries which are involved in chronic perioophoritis occasionally undergoes squamous metaplasia.⁶ Then there is the condition known as cystic fibrosis of the pancreas in which, due to the impaired absorption of fat-soluble vitamin A, there is a pronounced squamous metaplasia of the bronchial mucosa.⁷ It would appear, therefore, that squamous metaplasia is really of rather frequent occurrence in a wide variety of pathologic processes, running the gamut from chronic inflammatory lesions, and a vitamin deficiency state, to frank neoplasms. It seems entirely tenable, therefore, to assume that the squamous elements in the ovarian adenoacanthomas here in presented are, in fact, the result of the ubiquitous process of metaplasia.

Another plausible hypothesis for the presence of squamous epithelium in ovarian carcinoma is the supposition that such may result from Walthard's islands. According to Ewing,⁸ the latter are thought to result from the "invaginations of celomic epithelium." The manifold possibilities of celomic epithelium on differentiation are well known. It well may be that the origin of the squamous elements in ovarian acanthoma is identical with the generally accepted theory of histogenesis of Brenner tumor, viz., Walthard's cell rests.

Whether the squamous elements in the ovarian carcinomas described herein arise from squamous metaplasia or from Walthard's islands cannot be decided from our present-day knowledge of the histogenetic phenomena of the ovary. The authors, however, incline to the view that the squamatization seen in the tumors described is the result of metaplasia.

Summary

Two instances of a rare, primary ovarian neoplasm, adenoacanthoma, have been reported. The various histogenetic possibilities regarding the

origin of squamous elements in columnar epithelial carcinoma of the ovary have been discussed.

It is suggested that the term adenoacanthoma be used in naming these peculiar ovarian carcinomas, in keeping with the use of this term in the designation of adenosquamous tumors elsewhere in the body.

References

1. Ewing, J.: *Neoplastic Diseases*, 4 ed., Philadelphia and London, 1940, W. B. Saunders Company, p. 605.
2. Healy, W. P., and Cutler, M.: *AM. J. OBST. & GYNEC.* 19: 457, 1930.
3. Lindsay, W. S.: *Surg., Gynec. Obst.* 44: 646, 1927.
4. Meigs, J. V.: *Tumors of the Female Pelvic Organs*, New York, 1934, Macmillan Company, p. 144.
5. Novak, E., and Yui, E.: *AM J. OBST. & GYNEC.* 32: 674, 1936.
6. Novak, E.: *Gynecological and Obstetrical Pathology*, Philadelphia and London, 1941, W. B. Saunders Company, p. 331.
7. Anderson, D. H.: *J. Pediat.* 15: 763, 1939.
8. Ewing, J.: *Neoplastic Diseases*, 4 ed., Philadelphia and London, 1940, W. B. Saunders Company, p. 653.

OMPHALOCELE (AMNIOCELE)

Its Anatomy and Etiology in Relation to Hernias of Umbilicus and the Umbilical Cord

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THE incidence of omphalocele has been reported generally to be about 1:5,000 deliveries. This holds true for the case reported below, it being the second instance in 10,620 deliveries in this hospital since 1924. The first case was published by Jarcho,¹ who reviewed the literature on 400 cases to 1937. Since that time, more than 50 cases have been published, Ladd and Gross² alone reporting 22 cases from the Children's Hospital in Boston.

An unusual appearance for the obstetrician who encounters it for the first time, the cases look very much alike when one reviews the photographs published with the reports. In the typical omphalocele, the abdomen craniad to the supposed site of the navel is involved, never the lower abdomen. In many of the cases, there are no other malformations of the abdominal organs; smaller or larger parts of the small intestine and of the fetal liver are visible through, and during increased intra-abdominal pressure protrude into, an amnion-covered sac, the amount depending on the size of the defect in the abdominal wall which varies from 5 to 10 cm. in diameter.

The name "omphalocele" used for this congenital malformation by most of the authors in the latest publications (although "amniotic hernia" or "amniocele" would be more appropriate) should be applied to this anatomical and formational entity involving the supra-umbilical part of the abdomen, to differentiate it from a hernia into the umbilical cord in which a single loop of intestine, liver or omentum protrudes through a small ring into the cord, and from the true umbilical hernia covered by skin. As discussed later, these different structural defects do not seem to be simple gradations of the same condition, but originate at different stages of the developmental periods of embryonic life.

There is now a consensus of opinions that the only feasible way to save the life of the infants born with omphalocele is a surgical repair as soon as possible. The results depend on the skill of the surgeon, on

the time elapsed between birth and operation (at the latest 36 hours, because the thin amniotic membrane must not be allowed to dry out), and on the size of the sac. Ladd and Gross² point out that in their large series, they had 75 per cent survivals in patients with a sac less than 8 cm. in diameter, and only 15 per cent when the sac was larger than 8 cm. in diameter. The babies tolerate the open ether anesthesia very well and, where the approximation of the edges of the recti muscles is possible and will not be carried out too far cranial so as to interfere with the baby's breathing, which becomes impaired anyhow by the increased intra-abdominal pressure, the patients will most probably survive.

Case Report

A male, full-term, 8-pound, 4-ounce baby, was delivered by elective low-flap cesarean section on January 6, 1944. (Case history 81565.) The indication for the cesarean section was a double footling presentation in a 38-year-old, white, para 0, gravida ii. The pregnancy was uneventful and closely watched because the patient had gone through a period of essential hypertension up to 170/100, during several months subsequent to a pyelotomy for removal of a stone in October, 1941. She followed the contraceptive advice until normal blood pressure was established for 6 months. During the last trimester of the pregnancy, the fetal heart was always arrhythmic, of an extrasystolic type.

The delivered baby showed a huge, rounded defect in the abdominal wall occupying almost the entire upper and midpart of the abdomen, and covered by a thin translucent amniotic membrane in an area 10 by 8 centimeters. The umbilical vessels ran between the amniotic membrane and the peritoneum, and converged in the left lower quadrant to form a normal umbilical cord. Through the moist transparent membrane one could differentiate the left lobe of the liver in the upper part, and coils of small intestine in the lower part, of the defect. When the baby cried, the liver and the intestine became eviscerated into the sac, the bulging attaining the size of a large orange. During the crying, there was, moreover, a bulging of the skin-covered part of the epigastrium showing the complete diastasis of the recti muscles. The abdominal skin seemed abundant and creased around the sac and separated from the amnion by the physiologic red demarcation line. The anus was open and contained meconium. The baby seemed otherwise very well developed, and showed no other malformations except for an arrhythmic heart action. The umbilical cord was tied and cut, and a sterile dressing applied. Twenty-four hours later, the baby was operated on by Dr. A. Salvin under open ether anesthesia. The brim of the skin was circumcised and the fascia of the recti muscles freed. The recti abdominis muscles showed a complete diastasis in their upper thirds and converged toward the midline to unite right below the mid-abdomen. The peritoneum was entered, its margin circumcised and removed together with the membrane covering the evisceration. The closure of the gap, although difficult, was then accomplished in vertical direction (the liver was not adherent). A second row of enfolding fascial sutures was placed, and the skin approximated with silk sutures.

During the operation and with the dressing afterward, pains were taken not to interfere with the baby's breathing. Thus, the upper edges of the recti were not approximated and the dressing was loosely applied over the thorax.

The baby was put into an incubator with oxygen supply, 20 c.c. of maternal blood injected intramuscularly, several hypodermoclyses of 5 per cent glucose in saline 100 c.c. each time given during 48 hours. Mouth feeding was resumed on the third postoperative day, $\frac{1}{2}$ ounce of formula every 2 hours day and night, and increased by $\frac{1}{2}$ ounce every second day. Highest rectal temperature was 101.2° F. on the second postoperative day, and became normal from the fourth day on. Weight dropped to 7 pounds, 6 ounces on the fifth postoperative day, and from the seventh day on, the baby gained constantly and weighed 7 pounds, 12 $\frac{1}{2}$ ounces on the day of discharge. The extrasystoles disappeared

after a few days and an EKG taken 6 days post partum showed: Sinus tachycardia, rate varying from 136 to 160 in the various leads. P-R interval 0.10 second. Right axis deviation. QRS of low amplitude in the limb leads. Q-3 present. RS-T segment depressed in leads IV and V. T-I iso-electric, T-R low, T-4 and T-5 inverted: the abnormalities noted probably due to a poor functional state of the cardiac muscle. Unfortunately the EKG has not been repeated.

Mother and child were discharged in good condition on the thirteenth day after delivery. Seen last, 5 weeks after the operation, the baby weighed 9 pounds, 12 ounces. The abdominal wound healed by primary union and the repair of the omphalocele was in good condition. There was only a shallow pit below the ensiform process during inspiration and crying. Heart action was regular.

Follow-up Note.—While this paper was being prepared, I was notified that the infant which had been growing and developing normally, suddenly died “apparently from an acute heart failure” on March 28, 1944. No autopsy was obtained.

Discussion

Lately, the conception on the formal genesis of omphalocele has changed from the assumption of the primitive intestinal loop failing to withdraw into the celomic cavity toward the end of the third month of embryonic life (Jarcho¹), to the explanation that the cause may arise from a disparity between the size of the abdominal viscera and the abdominal cavity, resulting from a retarded development of the abdominal parietes. (Bergglas,³ Gross and Blodgett,⁴ Ladd and Gross,² Specht and Shryock.⁵) Aside from reports on cases and discussions on the cause, there exist two large monographs on malformations of the ventral wall of the trunk, Kermauner's⁶ and Sternberg and Politzer's.⁷ Kermauner generalized the cause of all clefts of the ventral wall and related them to retardation of or fault in, development of the different metameres of myotomes which begin to spread ventrad from the primitive spine in the third week. He denied any correlation between the development of abdominal parietes and the withdrawal of the primitive intestine and also disapproved the idea, that increase or even excessive growth of the viscera could be a causative moment for the formation of a congenital hernia. By stating that “the amniotic covering of the hernial sac corresponds to the somatopleure, the lower membrana reuniens,” he accepts Aschoff's⁸ and Neugebauer's⁹ opinions that the covering of the upper part of this kind of hernia does not represent the dilated base of the navel, but that it corresponds to the upper part of the anterior abdominal wall, arrested in its development. Still he generalizes the causes of the different structural defects in the ventral wall of the trunk on the base of His' theory of conrescence of the two halves of the body in the ventral midline. He contends, however, that at that time (1909), “there is only little knowledge about the details on morphology of the definite closure of the abdomen.”

Since that time, two basically important papers on the formation and closure of the anterior abdominal wall in normal human embryos have been published (Pernkopf,¹⁰ Politzer and Sternberg¹¹). The last two authors examined the formation of the umbilical pedicle and that of the anterior abdominal wall on embryos from 2.3 mm. to 9.5 mm. length, while Pernkopf's paper deals with the formation of viscera and with closure of the umbilical ring in fetuses up to 50 mm. length. Politzer and Sternberg show that the ventral wall of the trunk is formed in a very complicated way in several portions: the pericardial, supra-umbilical, umbilical, subumbilical and genital parts and at different times. In their monograph,⁷ where they also report a case of omphalocele with severe other malformations, they discuss the formal genesis of malformation of the respective parts of the ventral wall of the trunk based on the knowledge derived from their first paper.

Due to the curling of the 1.5 mm. embryo, the anlagen of organs built from the mesodermal field as the heart and liver, rotate around a trans-

verse axis and parts which primarily lay cranial are shifted ventrad and then caudad. At the same time, the embryo is being enveloped by the amnion sac which ensheathes the body stalk and thus forms the extracelomic cavity. According to Politzer and Sternberg, there is one stage in this development (in embryos of 6 to 7.5 mm.) where the later cranial amniotic covering of the abdominal pedicle ("amniotische Deckplatte") forms the outer layer of and unites with, the transverse septum, a part of the mesodermal field from which a portion of the pericard is formed and into which the liver cells grow in. Later, in embryos of 9 mm. length, due to the prolific growth of liver cells on the dorsal part of the transverse septum and to proliferation of connective tissue from its ventral part, this amniotic covering has been shifted caudad to form the cranial covering of the umbilical pedicle. It thus gives way to the formation, from the transverse septum, of the supra-umbilical portion of the abdominal wall, which then consists of embryonic connective tissue covered by ectoderm.

This means that the later supra-umbilical part of the abdominal wall, the only part of the body surface save for the navel, has a transient covering of amnion and the two authors relate the origination of omphalocele to a disturbance in development of this amniotic covering. The close interrelation in the development of this amniotic covering, of the fetal liver and of the heart on, into and from the transverse septum, respectively, accounts for the presence of the liver in at least two-thirds of the cases and the frequent malformation or adhesions of the liver as well as for the defects of the heart, or even its presence in the gap.

The two authors do not try to explain how this disturbance in development may arise. In my opinion, the formational irregularity must lie in the relation of this amniotic covering to the underlying connective tissue of the transverse septum. Normally, the amniotic covering becomes closely adherent to the transverse septum in the earliest stage of their contact, although the two structures can be easily distinguished histologically even in the later stages. If, by mere chance, these two structures fail to conalesce, or if the connective tissue of the transverse septum fails to proliferate and thus to push the amniotic covering caudad toward the umbilical pedicle, an amnion-covered gap will be left open in this supra-umbilical part of the abdominal wall and result in the structural defect of an amniocoele.

At this stage of development (beginning of the third week), the myotomes have hardly started to spread ventrad. In the course of the sixth to eighth weeks, the abdominal muscles are differentiated from the myotomes and spread ventrad within the embryonic connective tissue which also serves to form the firm aponeurosis of the linea alba. In cases of the above-described aberration, however, the recti muscles are hindered to assume their normal relation, because there is no medium (connective tissue) in which they normally grow, and thus, they only surround the gap. Studies of Pernkopf¹⁰ show that the recti muscles do not take active part in the closure of the abdominal wall because long after retraction of the intestinal loops from the extracelomic cavity and after closure of the umbilical ring (fetuses of 50 mm. and more), the recti muscles still run V-shaped and are completely diastatic in their upper and midportions. The umbilical ring is formed by proliferation of the adventitial connective tissue of the umbilical vessels which process also aids the retraction of the extracelomic peritoneum. Moreover, according to Tandler,¹² the diastasis of the upper recti muscles is a physiologic feature in newborn and in young children. Based on these studies, we can discard Kermauner's hypothesis that all malformations of the anterior wall of the trunk are caused by an arrested or retarded development of the corresponding myotomes. The same applies to the assumption of others, that the formation of an omphalocele may be due to a disparity between the size of the abdominal viscera and the abdominal cavity resulting from a retarded development of the ab-

dominal parietes because, once the supra-umbilical part of the abdominal wall has been formed normally, no herniation covered by amnion can develop on this spot.

We can also relinquish the view that an omphalocele is due to the failure of the primitive intestinal loop to withdraw into the abdominal cavity, because omphalocele is a malformation of the supra-umbilical portion of the abdominal wall and not one of the umbilicus proper.

Real hernias into the umbilical cord are caused by either a failure of the abdominal contents to retract from the extracelomic cavity at the right time, or by a failure in the proliferation of the adventitial connective tissue of the umbilical vessels with resulting primary hernial sac and secondary herniation of the abdominal contents. Both aberrations occur as can be judged from cases of incarceration of intestine or liver in congenital umbilical hernia (failure of withdrawal at the right time and normal proliferation of connective tissue), or from cases of free hernias (failure of proliferation of connective tissue and of retraction of extracelomic peritoneum). The time at which these hernias develop is the eighth to tenth weeks (fetuses of 45 to 50 mm. length) and as the supra-umbilical part of the abdomen had been formed normally in the third week, these cases show normal anatomy of the upper abdominal aponeurosis and the recti muscles.

We must, of course, realize that the omphalocele always involves the umbilical region of the abdominal wall. In the same way as the lack of connective tissue hinders the approximation of the recti muscles, it causes also the cranial circumference of the umbilicus proper to remain open. The extracelomic cavity cannot be closed in its upper part because it lacks on this spot in connective tissue which in normal cases is derived from the ventral part of the transverse septum, the later supra-umbilical part of the abdominal wall. But immediately below the navel, the recti muscles are completely approximated which proves that the different portions of the abdominal wall are formed independently.

Summary

1. A case of omphalocele is reported, operated 24 hours after delivery, with recovery.

2. Etiology of amniocoele is discussed and assumed that it may be due to either a failure of union of the mesodermal transverse septum with its amniotic covering, or to a failure in proliferation of embryonal connective tissue in the transverse septum, processes in the third week of embryonal development, which normally lead to formation of the supra-umbilical part of the abdominal wall.

3. Omphalocele (amniocoele) is defined as an anatomical and formational entity, a malformation of the supra-umbilical part of the abdominal wall and is differentiated from hernias into the umbilical cord.

4. The time of origin of this structural defect is confined to the third week of embryonal development, contrary to formation of hernias into the umbilical cord which develop in the eighth to tenth weeks.

References

1. Jarcho, J.: Surg., Gynec. & Obst. 65: 593-600, 1937.
2. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, 1941, W. B. Saunders Co.
3. Bergglas, B.: Arch. f. Gynäk. 152: 214, 1933.
4. Gross, R. E., and Blodgett, J. B.: Surg., Gynec. & Obst. 71: 520-527, 1940.
5. Specht, N. W., and Shryock, E. H.: Surg., Gynec. & Obst. 77: 319-325, 1943.
6. Kernauner, F.: Die Missbildungen des Rumpfes, in: Schwalbe, Die Morphologie der Missbildungen, Jena, 1909, G. Fischer.
7. Sternberg, H., and Politzer, G.: Beitr. z. path. Anat. 88: 150, 1931.
8. Aschoff, L.: Virchow's Arch. f. path. Anat. 144: 511, 1896.
9. Neugebauer, L.: Monatschr. f. Geburtsh. u. Gynäk. 20: 1219, 1904.
10. Pernkopf, E.: Ztschr. f. Anat. 77: 1925.
11. Politzer, G., and Sternberg, H.: Ztschr. f. Anat. 92: 279, 1930.
12. Tandler, J.: Lehrbuch der Anatomie, Wien, 1922, J. Springer.

A RECTAL MANEUVER FOR PLACENTAL DELIVERY

With Observations on Rectal Palpation in the Third Stage

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THE determination of the presence or absence of the placenta in the birth canal and its delivery therefrom if incarcerated, can be accomplished rectally.

It is often difficult to determine the location of the placenta during the third stage. The classic signs of placental separation usually disclose whether the placenta has separated or not, but they do not tell whether the placenta is being harbored by the uterus, or by the vagina. When

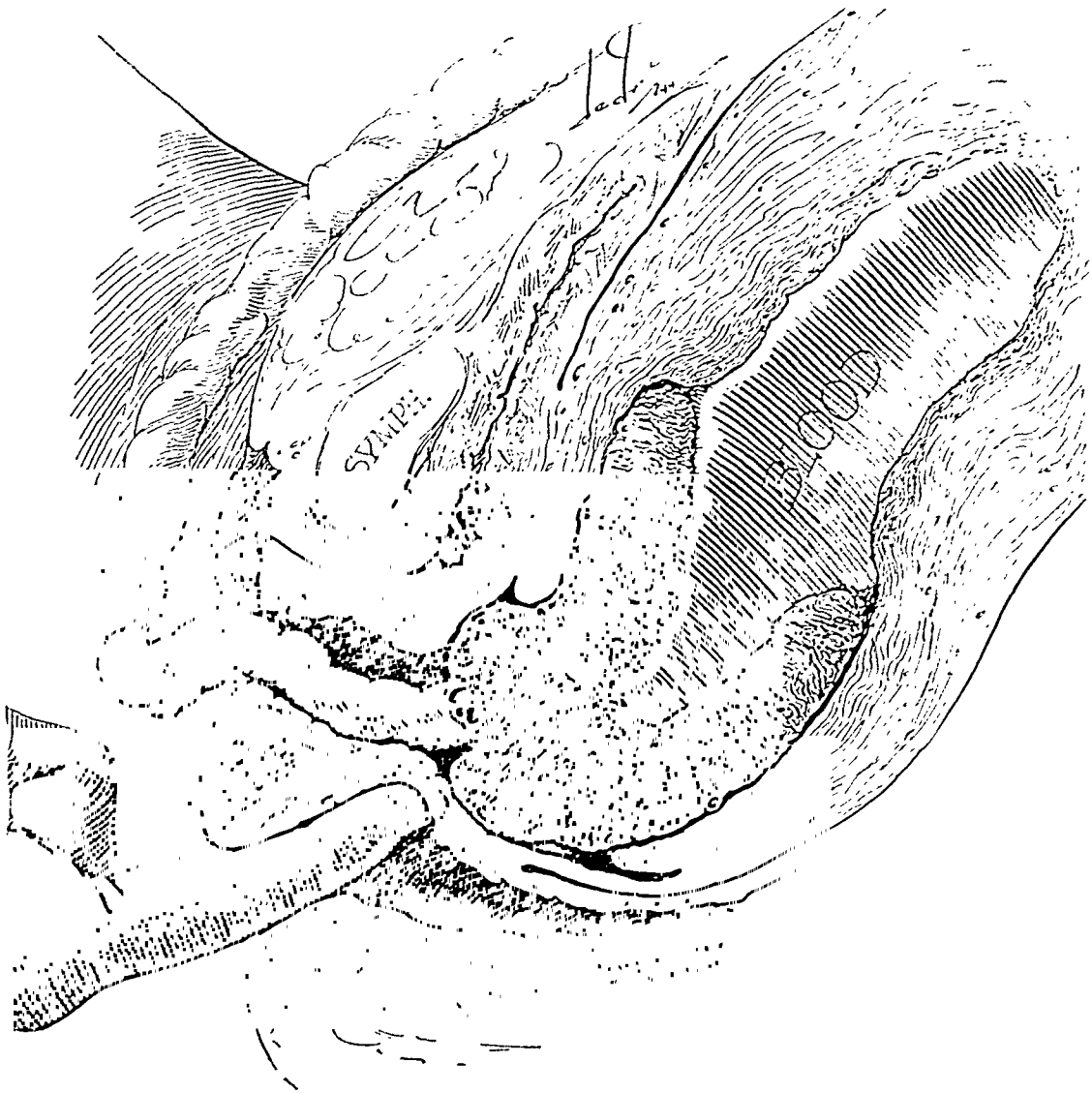


Fig. 1.—Diagnostic rectal palpation.

placental delivery is delayed, this is often a perplexing problem, and one that invites promiscuous vaginal examinations in the third stage. The vaginal examination reveals, of course, whether the placenta is intra- or extrauterine, but each vaginal examination is an invitation to puerperal infection, and any method which would reveal the same information



Fig. 2.—Rectal maneuver, step one: Hooking finger around placenta.



Fig. 3.—Rectal maneuver, step two: Milking out the placenta by a stripping action.

without the danger of infection should be the one of choice. Such a method is readily available by employing rectal examinations (Fig. 1). Many unnecessary vaginal examinations would be eliminated if, prior to attempting a manual removal of the placenta in a prolonged third stage, a rectal examination were done to more definitely establish the location of the placenta.

Rectal examinations in the third stage not only are useful for establishing the location of the placenta, but also for permitting placental delivery by the examining finger, in the following manner: the finger is hooked around the placenta (the anterior rectal and posterior vaginal wall intervening between finger and placenta) and the placenta is milked out by a stripping action. (Figs. 2 and 3.)

Rectal delivery of the placenta is particularly useful in cases of delayed placental delivery due to placental incarceration in a birth canal which has a small primiparous introitus, or one which has been narrowed by a recently sutured episiotomy. Moreover, in cases of placento-vaginal disproportion due to oversized placenta, the placenta often requires vaginal extraction; such placentas can usually be delivered by rectal stripping. Delivery of the placenta by rectal stripping is also indicated in cases of atony of the multiparous pelvic floor, especially following prolonged anesthesia. A retained, separated placenta is not an infrequent complication of the administration of ergotrate prior to placental delivery. When the greater part of the placenta is retained by a tight lower uterine segment, the rectal maneuver will not suffice; when, however, the greater part of the placenta is in the vagina, and only a small part is retained in the uterus, then rectal stripping will usually deliver the placenta.

Summary

1. A rectal maneuver for aseptic delivery of the placenta incarcerated in the lower birth canal is presented.
2. The maneuver consists of hooking the examining finger around the placenta and milking out the placenta by a stripping action of the anterior rectal wall.
3. This procedure is advocated only when complete uteroplacental separation has previously taken place, and when delay in placental delivery is due to one of the following: (a) tight introitus, (b) placento-vaginal disproportion, (c) atony of pelvic floor, or (d) spastic cervical segment due to previous administration of ergotrate, partially retaining the placenta.
4. This method of placental removal is not advocated for routine management of the third stage.
5. Diagnostic rectal palpation in the third stage is recommended in cases of delayed placental delivery, because it is as informative as a vaginal examination without the associated risk of bacterial contamination.
6. In cases of delayed placental delivery, a rectal examination should be done to confirm the location of the placenta before attempting a manual removal.

The author wishes to express his thanks to Dr. Clyde L. Randall for his encouragement and advice, and to Mr. Melford Diedrick for the illustrations.

THE DIFFERENTIAL DIAGNOSIS BETWEEN FETAL AND MATERNAL HEART RATE

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IT IS not infrequent when listening to the fetal heart rate for doubt to arise whether what one hears is really the fetal rate, or that transmitted from the mother's heart. This particularly is noted in cases where there is a rapid maternal rate—100 to 140—which is not at all uncommon during labor, notably in the protracted ones with exhaustion. Difficulty most often arises when the maternal apex beat or pulse rate and the fetal heart rate are exactly alike. The question then presents itself as to whether we are dealing with a live fetus, or one that is dead with a transmitted maternal heart rate over the uterus.

The author has used the following technique for a number of years with gratifying results. It is based on the phenomenon of the respiratory arrhythmia. As is well known, the normal beat accelerates during inspiration and slows during expiration. This is due to a decrease of vagus activity with acceleration of the heart beat during inspiration, and an increase of vagus activity with slowing of the heart during the expiratory phase.

While listening to the fetal heart, preferably with the head stethoscope, the maternal pulse is palpated. Let us assume both rates to be the same. The mother is asked to take a deep breath and then to exhale forcibly and completely. During this expiration, it will be noted that the maternal pulse definitely slows up during the subsequent two or three beats. This slowing, of course, does not affect the fetal heart which continues to beat at its regular rate and rhythm. On the other hand, should the heart sounds over the uterus slow simultaneously with the slowing of the maternal pulse, then we are dealing with transmitted maternal heart sounds. The deductions in both instances are obvious—a live baby in the first instance, and one with absent heart tones in the latter.

Conclusions

A small point in the differential diagnosis between maternal and fetal heart rates is described. The technique takes advantage of the respiratory arrhythmia (sinus arrhythmia) of the mother. It has proved helpful in a number of doubtful cases.

The data upon which this paper is based have been collected during civilian practice.

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American Obstetric Services

THE CHICAGO LYING-IN HOSPITAL

THE Chicago Lying-in Hospital and Dispensary was founded by Dr. Joseph B. DeLee in 1895. A four-room flat at 1336 Newberry Avenue was opened on Feb. 14, 1895, as the first dispensary. The first home delivery was on Feb. 27, 1895. In October, two medical students began to live at the dispensary. In 1896 a training school for nurses was started and the first intern began working at the dispensary.

A house at 515 Ashland Boulevard, with a capacity of nine beds, was opened on Sept. 2, 1899, as the first maternity hospital, and the first hospital delivery was on Sept. 14, 1899. Many of the leading obstetricians and pediatricians of Chicago helped staff the dispensary and hospital.

A three-story building was completed in 1904 on the corner of Maxwell and Newberry Streets, which became known as the Maxwell Street Dispensary of the Chicago Lying-in Hospital.

A new building, the Mothers' Aid Pavilion (isolation unit) with a capacity of thirty beds and bassinets, was opened on Nov. 6, 1914. It was used as the maternity hospital until the main building with a capacity of 140 beds and 120 bassinets was opened in 1917. Approximately 3,000 women were delivered each year after completion of the main building.

The hospital in 1927 became affiliated with the new medical school of The University of Chicago. A new hospital and Mothers' Aid Pavilion located on the Midway were opened on May 29, 1931. The hospital is adjacent to the Albert Merritt Billings Memorial Hospital and other hospitals belonging to The University of Chicago Medical School.

The main building of the Chicago Lying-in Hospital is six stories high, containing 143 beds and 119 bassinets. There are nine labor rooms, four delivery rooms, and an operating amphitheater on the fifth floor. The sixth floor contains quarters for the interns and residents. There is a separate nursery for premature babies.

The Mothers' Aid Pavilion (isolation) is an adjoining three-story building containing 24 beds and 18 bassinets, a delivery and an operating room. The departmental research laboratories, library, and private patient offices are also in this unit.

The adjoining clinic building, known as the Max Epstein Clinic building, contains ten examining rooms with adequate clinical laboratories, basal metabolism room, and fluoroscopic and dental equipment.

The Women's Board of the Hospital, on July 1, 1938, deeded the hospital and its assets to the University. The Boards, both of the

Beginning with the article on "The Lying-In Hospital of New York," published in the February issue, the JOURNAL is presenting brief descriptive articles dealing with the leading institutions devoted to the care of obstetric patients. These articles will review the history, equipment, staff, and similar features, affording to our readers certain general activities of hospitals in this field of practice. We trust that interest and value.

The Editor.

Lying-in Hospital and of the Mothers' Aid Pavilion, have continued to serve in an advisory capacity and have also continued their financial support of both institutions.

The supervision and support of the Maxwell Street Dispensary were stopped by the hospital on June 30, 1932. However, it was continued by Dr. DeLee as the "Chicago Maternity Center." A home delivery service using the hospital as a base was opened in November, 1932. This was discontinued in March, 1943, because it was felt that better care of the patient and better teaching of student, intern, and nurse could be carried out in the hospital than in the home.



Fig. 1.—Chicago Lying-in Hospital, Mothers' Aid Pavilion, and Max Epstein Clinic Building.

The departmental staff before the war consisted of a professor, two associate and two assistant professors, four instructors, and four research associates, each a Ph.D., who supervised their respective laboratories—pathology, bacteriology, chemistry, and endocrinology. The house staff comprised six residents (four-year training) and sixteen interns (nine-month training), each of whom had had one or more years of hospital training prior to appointment. On April 1, 1943, first-year interns were accepted for a period of three months, the remainder of their time being spent in the other hospitals of The University of Chicago. The present staff consists of two professors (one is Chairman of the Department and Chief of Staff of the hospital), one associate and one assistant professor, an assistant professor of pathology, a research associate (Ph.D.) in chemistry, one instructor, and three instructors on leave of absence in the Armed Forces.

The courtesy staff consists of ten specialists in obstetrics and gynecology, known as the "Associate Staff," and approximately thirty additional doctors, some of whom are specialists, who comprise the eligible staff. These men have the privilege of bringing private patients to the hospital and participating in departmental conferences, but have no responsibility for teaching or care of staff patients.

The consultants for the hospital are the other heads of departments of the medical school.

The obstetricians retain control of the babies, but all care of the newborn baby is directed by members of the department of pediatrics of the University or qualified private pediatricians if the patient is a private patient.

The hospital has well-organized clinical laboratories and a department of pathology, which is under the direction of the professor of pathology in the medical school. The department of obstetrics and gynecology has its own special laboratories (chemistry, bacteriology, endocrine, and pathology) for research work and animal experimentation. The complete facilities of the basic science departments of the medical school are also available for special study and research. The hospital maintains its own diagnostic x-ray department under the supervision of the professor in the medical school. At Billings Hospital deep x-ray therapy is available, and the O. C. Miller radium clinic located in that hospital has 183 milligrams of radium in various applicators, suitable for the treatment of gynecologic patients.

The medical library of the hospital is a part of the University Libraries. It contains 3,800 volumes pertaining to obstetrics and gynecology and subscriptions to thirty special surgical journals and periodicals. A full-time librarian is in charge.

Almost half of the rotating intern's obstetrical service is on the birth room floor. The remaining time is given to the antepartum and postpartum care of women both in the clinic and the hospital, and to the care of the newborn under the direction of members of the department of pediatrics.

Graduate Training in Obstetrics and Gynecology

The department conducts well-organized prenatal and postnatal clinics, gynecologic clinics, and other special clinics for the care of these patients (toxemia, anemia, endocrine, sterility, lower genital tract infections, lipiodol visualization, tumor, maternal guidance, etc.).

First Year of Training.—Junior residents are limited to obstetrics, and at least one year of basic internship or its equivalent is required for the appointment. Two or more appointments are made quarterly on the recommendation of the chairman of the department. The first six months of the service are spent primarily in the clinic and hospital care of normal and abnormal pregnant and postpartum patients, some gynecologic patients, emergency anesthetics (the hospital has six full-time anesthetists) and newborn pediatrics. There is no home delivery service. The last three months are spent in the birth rooms where each resident is trained in the conduct of the third stage of labor, in the use of forceps, and the technique of episiotomy. He also assists the staff with private and abnormal cases. Full maintenance plus an annual stipend is provided. A health examination in our clinics is required before final acceptance.

Further appointments made each January and July to senior and chief residencies are based on the applicant's knowledge and clinical ability as shown during his junior residency. Full maintenance is provided during the residency plus an annual stipend which increases

from year to year. Each man is urged to participate in some research work. Following the chief residency an appointment may be made as instructor, usually on January 1 or July 1. The term of this appointment is for one year with full maintenance plus a salary.

The full-time departmental staff closely supervises all of the activities of the resident staff. The senior staff, consisting of three professors, rotates on the obstetric and gynecologic service, having a junior staff man as an assistant.

Second Year of Training.—During this year the senior resident will be first assistant to one of the senior staff in the care of his private and staff patients. All of his work will be in the Lying-in Hospital, the Mothers' Aid Pavilion, and the near-by Billings Hospital. He is responsible for the care of the patients under him as well as the supervision of the work of the intern and students on his service. Staff rounds are made daily.

Third Year of Training.—In the third six months the resident works full time in the various special laboratories of the department. He is taught the fundamentals in each of the laboratories. During the last half of the year the resident is in charge of the waiting and post-partum obstetric patients. He makes daily rounds with the obstetrician in charge and with the interns and the medical students. He assists in the delivery rooms.

Fourth Year of Training.—During the first six months the resident is in charge of the gynecologic service and arranges the daily operating schedule. He operates under the supervision of either the senior or junior staff gynecologist and at the end of this period is competent to perform major gynecologic surgery. He makes daily rounds with the gynecologist in charge of the service and with the senior residents, interns, and students.

During the last six months he is in charge of the obstetric service. Most of his time is spent on the delivery floor but he is held responsible for the care of all the obstetric patients in the hospital. He, with the assistance of two of the senior residents, must be present at all deliveries. At the end of his training he is a competent obstetrician and gynecologist and is qualified for certification by the American Board of Obstetrics and Gynecology.

Organized Study.—The department of obstetrics and gynecology holds weekly clinical conferences, conducted by the chairman of the department, for a review of the clinical work. Selected cases are reviewed, autopsy material is presented, and departmental problems are considered. The residents have an active part in preparing the programs for these conferences, presenting cases, and participating in the discussions. Facilities of the library are fully utilized in the preparation of these presentations.

Teaching Activities.—Each member of the resident staff has an active part in assisting the members of the faculty and the head of the department in supervising the clinical clerkships, in presenting cases when teaching rounds are made, and in assembling the material for the various teaching clinics. The senior and chief residents assist in teaching nurses and medical students.

Higher Medical Degrees.—No examination or thesis is required for the individual undertaking the usual course of graduate training in obstetrics and gynecology. If he is a candidate for a higher degree, either a Master's or Doctor of Philosophy, he must then comply with the prescribed requirements as to fundamental training and investigative work and must meet the requirements of the American Board of Obstetrics and Gynecology.

Pertinent data as to the number of deliveries, incidence of operative deliveries, and various major obstetric complications, as well as the maternal and fetal mortality are given in Table I, A. Our maternal and fetal mortality compare very favorably with other maternity hospitals. The hospital staff has always believed in prophylactic or out-

TABLE I
A. OBSTETRICS

(NUMBERS OR PERCENTAGE)				
	1931-1941	1941-1942	1942-1943	1943-1944
Deliveries, 400 + Gm.	27,321	3,236	3,813	3,581
Abortions, less than 400 Gm.	900+	57	69	173
Maternal mortality, total	(50) 0.177	(4) 0.124	(4) 0.105	(2) 0.056
Morbidity, per cent		8.0	8.8	8.4
Operative deliveries, per cent	33.0	41.5	55.0	45.0
Cesarean sections, 400 + Gm.	1,457	147	166 a	151 a
Maternal Mortality	10	1	0	0
Breech deliveries, per cent	3.8	4.3	5.2	2.7 b
Postpartum hemorrhage, per cent			87	104
Twenty-four-hour postpartum tubal ligation			42	38
Obstetric operations—not delivery	1,029+	268	283	277
FETAL RESULTS—PER CENT				
Premature deliveries	6.2	7.0	7.5	6.2
Stillbirths	2.26	1.83	1.96	1.62
Term—2500 + Gm.	1.06	0.77	0.79	0.78
Premature—1,000–2,499 Gm.	0.90	0.77	0.87	0.56
Previa—400–999 Gm.	0.29	0.29	0.32	0.28
Neonatal deaths	2.03	1.68	1.70	1.65
Term	0.70	0.31	0.55	0.56
Premature	1.06	0.83	0.95	0.84
Previa	0.26	0.52	0.20	0.25
INCIDENCE				
1931-1944	MORTALITY			
	INCIDENCE	MATERNAL NUMBER	PER CENT	FETAL PER CENT
Noneconvulsive toxemia and/or hemorrhage, nephritis infection, heart disease	8.1	2	0.06	11.0
Eclampsia	0.22	9	0.29	
Placenta previa	0.63	4	5.8	26.0
Abruptio placentae	0.59	2	0.77	28.0
Postpartum hemorrhage	2.9	3	1.33	62.0
Cesarean section	4.74	4	0.36	
Abortion—up to 399 Gm. or 22 weeks	3.00	11	0.61	*8.7
		2	0.17	
Uncorrected figures for all pregnant women admitted. 37,951 deliveries of 400 + Gm. 1,199 abortions—less than 400 Gm. or 22 weeks. a: 1,500 + Gm. b: 2,500 + Gm.				
B. GYNECOLOGY				
Operations	6,216	640	555	518
Mortality—includes terminal carcinoma	65	6	3	5

let forceps (for the benefit of the patient and baby as well as for teaching), which explains the high incidence of operative deliveries.

The major portion of the operative gynecology is performed at the Lying-in Hospital in separate operating rooms. A small number of patients are cared for in Billings Hospital. Pertinent data are given in Table I, B.

The general and private clinics are in use every day except Saturday afternoons. Two thousand patient treatments are given each month in the general clinic (for teaching) and 1,000 in the private clinic.

The students, interns, residents, and departmental staff examine patients in the general clinic. The delivery rooms are open at all times to our medical students and house staff.

WILLIAM J. DIECKMANN, M.D.

Department of Reviews and Abstracts

Selected Abstracts

Pregnancy, Physiology, Diagnosis

Buxton, Russel: False Negative Results in the Friedman Test for Pregnancy, Virginia M. Monthly 71: 303, 1944.

Reports of negative Friedman tests have been found accurate in only 70 per cent of patients followed up at the Buxton Hospital since 1940. In 34 tests, the total number of errors was eight. In one the wrong urine was brought in for testing, in another the urine was collected in the afternoon, and in two others no cause for error could be ascertained. Four false negatives were found in patients who were taking estrogen therapy. These cases are reported in detail. As further confirmation of the fact that estrogen will induce a false negative test in the presence of pregnancy, a patient was selected who was known to be pregnant. A positive Friedman test was obtained and then the patient was placed on 40,000 units of Theelin in 7 days. The test became negative under estrogen therapy but the pregnancy persisted.

WILLIAM BICKERS.

Beruti, J. A., Leon, J., and Tenconi, E.: New Contribution to the Study of Transverse and Oblique Positions With Special Reference to Their Roentgen Diagnosis, Prensa méd. argent. 30: 2003, 1943.

The authors observed 14 cases: 11 transverse and 3 oblique. They show that the classic concept that in the transverse position the back of the fetus is always directed anteriorly or posteriorly is incorrect.

To avoid confusion, the authors accept the eight following varieties: anterior, anterosuperior, anteroinferior, posterior, posterosuperior, posteroinferior, superior and inferior.

Roentgen diagnosis is easy for the pure superior and inferior varieties, and the length of the images of the ribs passing beyond the vertebral column may reveal the degree of rotation of the fetus on its longitudinal axis. It is claimed by some that the anterior or posterior position of the back cannot be recognized. But if two films are taken, one in normal and the other in oblique exposure, it is easy to make the differential diagnosis.

Five of the 11 transverse positions were of the dorsosuperior variety. It seems that puriparity plays an important part in the etiology of this variety. The tendency to spontaneous change and the ease with which external version is performed are especially notable in the dorsosuperior variety and this applies also to the anterosuperior and posterosuperior ones. This explains why these varieties have been so seldom recognized clinically in the course of labor. On the other hand, spontaneous transformation of the transverse position into a longitudinal one never occurs in the frank dorso-anterior and dorsoposterior varieties.

The prognosis of the varieties in which the transverse position is corrected is favorable, provided that there is no anomaly in the pelvic canal. If the dorso-superior position persists, the mother runs the risk of premature rupture of the membranes, and prolapse of the cord is frequent and increases greatly the fetal mortality. When some mechanical obstacle is the cause of the dorso-anterior or dorsoposterior position, internal version and especially extraction by the natural route are made difficult and the fetal mortality is high; abdominal cesarean section is indicated in these cases.

The obstetrician must know the different varieties to guide him in performing internal version: he must bring down the lower foot in a dorso-anterior position, the upper foot in a dorsoposterior and the anterior foot in a dorsosuperior.

In any oblique presentation, the back of the fetus may offer eight different varieties as in the transverse presentation.

J. P. GREENHILL.

Chavanne, F. C., and Pittaluga, L.: Multiple Pregnancy, *Semana méd.* 50: 543-547, 1943.

The authors reviewed 257 multiple births observed in 18,129 labor cases seen at the Instituto de Maternidad of Buenos Aires from 1934 to 1942. There were 252 twin births and 5 triplets; i.e., twins occurred once in 72 births and triplets once in 3,626. One hundred thirty-two of the mothers were Argentinians, 125 were foreign. There were 88 primiparas and 169 multiparas. Among Argentinian women, twins occurred most often from age 20 to 25, and among foreign women (mostly Spanish and Italian) from 30 to 35 years. Two of the 257 patients died, a maternal mortality rate of 0.78 per cent. One of these deaths was due to amniotic infection, but the other was due to meningitis which was present before the onset of labor. In five instances, multiple pregnancy was repeated in the same mother. Forty per cent, or 109 women, were members of prolific families, with at least five brothers and sisters. Only six were nonsiblings. Family histories showed multiple pregnancies in 12 per cent, but this figure is believed to be lower than the actual number, because many women ignore the presence of twins in their family and even more in their husband's family.

Twin pregnancies are accompanied by more complications than single ones. There is greater distention of the abdomen, frequent hydramnios, and frequent edema, and above all, greater frequency of toxemia. In 17,862 single pregnancies toxemia occurred in 454, or 2.54 per cent, while in 257 multiple pregnancies, there were 26 cases of toxemia, or 10 per cent. The incidence of eclampsia in the first group was 0.34 per cent, while in the 257 multiple pregnancies, there were three cases, or 1.16 per cent.

In the 17,862 single pregnancies, 87 per cent were at term, while only 40 per cent of the multiple pregnancies were at term. The proportion of stillbirths was twice that of single pregnancies; 8 per cent contrasted with 4 per cent. In the 252 twin births, presentation of both fetuses was cephalic in 41.27 per cent; one cephalic, the other podalic, in 40.4 per cent; both podalic, 8.33 per cent; one cephalic, one shoulder, 3.9 per cent; one podalic, one shoulder, 2.7 per cent; and both transverse, 0.39 per cent. Forty-one operations, or 15.95 per cent, were required, contrasted with 6.15 per cent in single births. Of the 41 cases, five were forceps deliveries, 32 internal versions, two cephalic embryotomies and 18 pelvic extractions. There were 504 infants, 265 boys and 239 girls. In 169 births, both infants were of the same sex and 83 of different sex. Excluding stillbirths, 99 had died after two weeks, an infant mortality of 20.6 per cent.

In the 257 cases, the puerperium was normal in 70 per cent, subfebrile in 23 per cent and febrile in 7 per cent. These percentages are approximately the same as for single births, except for a slight increase in subfebrile puerperia.

J. P. GREENHILL.

Dragiff, David A., and Karshan, Maxwell: Effect of Pregnancy on the Chemical Composition of Human Dentin, *J. Dent. Research* 22: 261, 1943.

This study attempts to ascertain whether pregnancy has any effect on the ash, calcium, and phosphorus contents of the dentine of human teeth. Without selection, 31 teeth were extracted from pregnant patients at the Vanderbilt Clinic, and the teeth of the control group, 21 in number, were from nonpregnant females in approximately the same age group. A modification of the Shear and Kramer method was employed. A modification of the Fiske and Subbarow method was used for the phosphorus determination.

The results of the analysis indicated that no difference exists between the pregnant and nonpregnant group with respect to the calcium, phosphorus, and ash content of teeth. The authors conclude that there is no basis for the view that minerals are withdrawn from the teeth of human beings during pregnancy.

There is a brief but adequate review of experimental and clinical observations which reveals a difference in the conclusions regarding the relationship between pregnancy and the teeth.

HOWARD C. MOLOY.

Weisman, Abner I., and Coates, Christopher W.: The Frog Test (*Xenopus Laevis*) for Pregnancy, *West. J. Surg.* 52: 171, 1944.

The South African frog (*Xenopus laevis*) is really not a frog. It is an "Anuran amphibian." The female has the peculiar biologic habit of carrying the eggs throughout the year and extruding them only at mating, or after hormone stimulation.

Four ounces of concentrated morning urine in each patient is required. To 80 c.c. of urine twice the volume of acetone is added. The mixture is stirred and allowed to stand when the precipitated proteins and hormones will have settled to the bottom. The supernatant fluid is decanted, the residue dried and mixed with 3 c.c. of tap water and adjusted to a pH of 5.5. One cubic centimeter is injected in the dorsal lymph space. A positive test is connoted by extrusion of the eggs usually about 8 hours after injection. The accuracy is 98.9 per cent for diagnosis of early pregnancy.

WILLIAM BICKERS.

Sullivan, Charles: Diet in Pregnancy, *New England J. Med.* 230: 167, 1944.

It is the responsibility of the physician conducting prenatal care to make every effort to insure the physical stamina and constitutional adequacy of the newborn infant.

Eugenically, the parturient state calls for the very best from a nutritional standpoint that the civilized state can present, so that the growing fetus will have available the maximum and optimum material essential to assure generations free from anomalous deficiencies of growth, as in the teeth, female pelvis and so forth, without extracting too great a toll from the parent host.

The daily dietary requirements of the average woman are reviewed, and a basic list is presented of food elements that with minimal supplemental additions will provide for an adequate normal nutritive relation between the pregnant woman and the fetus.

JAMES P. MARR.

Pregnancy, Complications

Kunz, Arturo Carlos: A New Treatment of Eclampsia, *Bol. Soc. de obst. y ginec.* 22: 570-575, 1943.

A new treatment of eclampsia with "Derifilina," a compound of theophylline and oxyamine, is reported by the author. Its rationale is based on the theory that the eclamptic state results from angiospasm, producing in turn edema and cerebral ischemia, which is the direct cause of convulsions. "Derifilina" is a white crystalline powder easily soluble in water. The combination increases the effects of its two components; the dominantly diuretic action of theophylline through renal vasodilatation and its vasodilating action on coronary, cerebral and pulmonary vessels is compensated by oxyamine which suppresses the usual abrupt effects of theophylline on arterial tension. "Derifilina" has a double vascular action, direct peripheral vasodilatation and on the vasomotor centers. In patients it produces (1) a short period of hypotension; (2) a slight increase in pulse amplitude; and (3) after two to three hours a further slight hypotensive effect with diminution of the pulse wave which lasts several hours.

The classic Stroganoff treatment of eclampsia is essentially antispasmodic, but with less pronounced effect than that produced by "Derifilina." The author reports spectacular results in four cases. The drug (one ampule) was administered intravenously in 20 c.c. of hypertonic glucose solution. The effect is immediate. Even during injection the blood pressure may fall from 23 or 24 c.c. of Hg to 7½, 8 or 9 c.c., and convulsions cease immediately. Only in two cases did slight convulsions recur within five minutes of the injection. In three cases, treatment was continued with the classic Stroganoff technique which had been begun on admission and 0.015 gr. of morphine hydrochloride served to maintain the effect of "Derifilina." Injection was not repeated in any case because it was unnecessary. The author believes that cure might be obtained with repetition of the drug, without following the Stroganoff method, but prefers the combina-

tion, since the latter does not require the vigilance necessitated by the stronger drug. Blood pressure returned to 11 or 12 and remained at this level for 24 hours.

In the three cases whose treatment was continued with the Stroganoff method, contractions began and spontaneous parturition occurred 8 to 16 hours after initiation of treatment. In no case was it necessary to shorten labor by intervention, since the patient's condition indicated that normal delivery could be accomplished. The excellent results obtained with this treatment are the more remarkable because two of the four patients were in extremely serious condition; in one the level of uric acid in the blood was 80 mg., and in the other 114 mg., which generally indicates a fatal prognosis.

J. P. GREENHILL.

Araujo, J. Onofre: *Present Aspects of the Problem of Eclampsia*, Rev. de ginec. e d'obst. 37: 143-164, 1943.

The author states that of the three elements which accompany eclampsia (edema, hypertension and albuminuria, or better still proteinuria) the most constant and perhaps the only one is arterial hypertension. According to Irving and Eastman among others, it depends on generalized arteriolar spasms, demonstrated by the correlation between the pressure values and the examination of the retinal vessels.

The author discusses the gravidic factors of hypertension, dividing them into metabolic and neuro-endocrine. This discussion reveals one outstanding fact: the intimate connection of pregnancy toxemia of the last trimester with the hypertensive syndrome. All authors agree that the cause of the convulsive crisis is cerebral edema.

The treatment of eclampsia and of the hypertensive syndromes which occur in the gravido-puerperal cycle is best based on the classification of these clinical entities proposed in 1940 and accepted by the American Committee. Any hypertension beginning before the twenty-fourth week of pregnancy should be considered as not having its etiologic cause in pregnancy, and a systolic pressure of 140 with a diastolic one of 90 should be accepted as the limit of normal in the pregnant woman.

The prognosis must be considered from the fetal and maternal points of view. For the fetus, pregnancy toxemia is one of the most frequent causes of death, being exceeded only by syphilis.

The cause of death in eclampsia is myocardial insufficiency, acute edema of the lungs and pneumonia, in addition to cerebral and meningeal hemorrhage.

The best methods to evaluate the intensity of the toxemia are regular taking of the arterial pressure and examination of the fundus of the eyes. Wagener, studying the arterioles of the retina in pregnancy toxemia, demonstrated four consecutive phases: spastic narrowing of the arterioles, irregular constriction of the arteries, appearance of hemorrhagic foci, and of whitish spots and diffuse retinosis. When the arterial pressure is above 140 mm., 72 per cent of the patients show evident changes in the retinal arterioles: hemorrhagic foci suggest danger of permanent lesion and justify interruption of pregnancy.

The treatment of the hypertension and of the convulsions must be considered separately. That of the former may be medical, surgical or obstetric, while that of the latter must consist of combating the cerebral edema, detoxifying the organism if possible and providing rest for the sensorium. To reach this triple end, hypertonic serums, venesection and sedatives are used.

J. P. GREENHILL.

Fuster, M. Fernandez: *Experimental Eclampsia*, Bol. Asoc. méd. de Puerto Rico 36: 109-113, 1944.

A convulsive syndrome which cannot be distinguished from eclampsia was induced by Fuster in a nontoxemic primigravida by the injection, intravenously of 800 c.c. of a 10 per cent solution of sodium chloride. The author believes that this is the first time this has been accomplished. Based on this experiment and on various observations by several workers, he concludes that the signs and symptoms of the toxemias of late pregnancy are due to a retention of sodium chloride in the tissues in a higher concentration than is compatible with normal

physiologic processes. The convulsions are probably due to the irritating effect on the brain of the high salt concentration.

The author does not know the cause of the abnormal retention of sodium chloride, but he suggests as a possibility the action of placental hormones and/or of the adrenal cortical hormones.

J. P. GREENHILL.

Toxemia

Gonzales, J. B.: Puerperal Fever Postpartum Infection of the Genital Canal, *Semana méd.* 50: 1197-1206, 1943.

The author outlines the history of puerperal fever and theories concerning it and stresses that there has been too much interference with the natural defenses in management of this condition. He deplores the use of antiseptics, which have yielded, at best, only mediocre results. These unsatisfactory practices he attributes to faulty thinking that infection should be controlled from without, whereas, if natural function of the body is to be utilized, it should be controlled from within.

The author says that the concept of universal value of the defenses of the body is quite different from that of recognition of the existence of natural defenses, which forms the basis of a theory of absolute noninterference, recognizing that they never fail, that they always are efficient and that these never should be substituted by other agents. This does not mean that these defenses are always sufficient to repel a bacterial invasion, but it does mean that there is no superior method; it means that any treatment applied from without it not only useless, but harmful; it means furthermore, that any treatment applied from without will be inferior to that of autodefense, so that the prime condition must be that its action is not interfered with, and finally it means that almost always, but not always (from the medical standpoint) the result of natural defenses is to re-establish a healthy state. This fact is amply proved in practice, when the natural defenses are respected and adequately controlled.

J. P. GREENHILL.

Armand, M. F.: Early Rising in the Puerperium, *Obst. y ginec. latino-am.* 1: 688-698, 1943.

Armand is an advocate of early rising in the puerperium. An analysis of 200 cases in Haiti showed that early getting up prevents thrombosis and embolus, aids uterine involution, helps drainage of the lochia and fosters quick recovery of the patient. The author also employed early rising after such complications as hemorrhage from placenta previa, uterine atony and also after intrauterine manipulation. He did not observe a single case of inversion, prolapse or retroversion due to the early rising. He, therefore, strongly recommends early rising in the puerperium regardless of the type of delivery and the presence or absence of complications.

J. P. GREENHILL.

Gabastou, J.: Sulfonamide Therapy by the Transplacental Route, *Semana méd.* 50: 983, 985, 1943.

The author has reported six cases of sulfonamide therapy by the transplacental route. The technique consists of injection of 100 c.c. of 5 per cent prontosil into the vein of the cord ten or fifteen minutes after labor. The cases were selected according to rigid indications, i.e., they exhibited a definite state of intrapartum infection, and they had not received previous sulfonamide medication. Patients with premature rupture of the sac, or with prolonged labor, or in whom operative interference appeared necessary, as a prophylactic measure, received treatment either orally or parenterally, but not by both routes simultaneously.

The transplacental route was selected for patients showing severe infection, in order to produce a topical reaction. They all had a temperature of 39° C., tachycardia, dry skin, fetid vaginal secretions, and in some instances, evidence of

infection in the blood stream. All patients displaying these severe symptoms, who were treated with sulfonamide transplacentally, showed remission of sepsis and were dismissed from the hospital as soon as patients with a normal puerperium.

J. P. GREENHILL.

Salm, R.: The Occurrence and Significance of *Clostridium Welchii* in the Female Genital Tract, J. Obst. & Gynaec. Brit. Emp. 51: 121, 1944.

The author made 843 vaginal swabs during the puerperium on patients showing a rise of temperature above normal. *Cl. welchii* was isolated on 50 cases or 6 per cent. In 300 swabs from venereal disease cases, *Cl. welchii* was isolated in 7.67 per cent, and in 300 swabs from pregnant women undergoing treatment for leucorrhea, *Cl. welchii* was isolated in 6.33 per cent. Forty per cent of *Cl. welchii* cases belonged to the category of manual and instrumental interference. None of the patients died or was seriously ill. *B. coli* was present in 62 per cent, anaerobic streptococci in 34 per cent and hemolytic streptococci in 10 per cent. It appears likely that the origin of *Cl. welchii* and *B. coli* is from the bowel itself.

The incidence of *Cl. welchii* increases with the number of examinations and instrumentations, and it appears likely that some of these organisms can be introduced with medical supplies such as instruments, cotton, etc. In the absence of clinical signs, active treatment should not be instituted without clinical evidence that invasion has taken place.

WILLIAM BERMAN.

Lubin, S., and Horowitz, I.: Postpartum Hematomas, Am. J. Surg. 63: 272, 1944.

In reporting 4 cases of postpartum hematomas, the authors call attention to the seriousness of the condition if not recognized and treated early. They describe 2 types, the immediate and the delayed, either of which may involve the perineum, labia, vagina, base of the broad ligaments, and even the subperitoneal tissues to the kidney and diaphragm. The cause is necrosis of blood vessels as the result of pressure, tears, and inadequate hemostasis. Immediate evacuation of the hematomas in conjunction with measures to combat shock is the treatment of choice in most cases. All of the authors' case reports were of involvement of the vulva, vagina, labia, or perineum. The literature is reviewed.

FRANK SPIELMAN.

Timerman, H. J.: Postpartum Appendicitis, Am. J. Surg. 55: 138, 1942.

The author calls attention to the rarity of appendicitis in the puerperium and reports 2 cases. These were the only ones observed in 17,489 deliveries from 1916 to 1939 inclusive. The symptoms and pathologic findings were typical. Both cases reported followed the administration of strong cathartics.

FRANK SPIELMAN.

Bloom, O. H.: Suppression of Lactation by Stilbestrol, Am. J. Surg. 54: 443, 1941.

Stilbestrol was administered to 110 postpartum patients in order to obtain a suppression of lactation. The dosage utilized was 5 mg. of the preparation 3 times daily for 2 days. No other form of therapy was used; no restriction of fluids, tight binder, atropine, saline cathartics, etc. Successful suppression of lactation was achieved in over 90 per cent of the cases. No untoward effects were noted.

FRANK SPIELMAN.

Miscellaneous

Henry, Noel R.: The Rh Factor and Prognosis, M. J. Australia 2: 114, 1944.

The author reports a case of a woman whose first infant died on its thirteenth day of life from jaundice after having had several blood transfusions. In the next two years this woman had three miscarriages at three months, five months, and two months. No further pregnancy ensued for the next six years. The patient then became pregnant for the fifth time. She was given progestin and wheat germ oil.

She delivered a normal baby without any complications. The mother's blood belonged to group O and was Rh negative. The infant's blood was of group O and was Rh positive. (The father had to be Rh positive.) The author questions the significance of the six years of infertility, and feels that our knowledge is as yet incomplete to advise these women against future pregnancies.

WILLIAM BERMAN.

Simmons, R. T., Graydon, J. J., and Hamilton, Patricia: *The Rh Factor in the Blood of Australian Aborigines*, M. J. Australia 1: 553, 1944.

The authors collected blood samples from 281 pure-blooded Australian aborigines and four hybrids and these were all found to be Rh positive. The finding of the Rh factor in all pure-blooded Australian aborigines completes another link in the blood similarities of American Indians and Australian aborigines. The original stock of each race probably possessed only two blood groups, A and O, and all persons of group A belonged to subgroup A₁. The main difference in the blood of these two races is that the Australian aborigines have the highest, and the American Indians almost the lowest, type N percentages yet found.

WILLIAM BERMAN.

Necrology

LYLE G. McNEILE, M.D., obstetrician and gynecologist, of Los Angeles, California, died there March 1, 1945, at the age of 60 years. A graduate of the University of California in 1910, he established the Los Angeles Maternity Service, a maternity service of the city's health department, and was among the first members of the faculty of the University of Southern California when the Department of Obstetrics was organized in 1931, serving as instructor and professor until 1939. Dr. McNeile was a Fellow of the American College of Surgeons and a Diplomat of the American Board since 1930, but was retired from active practice.

HILLIARD EVE MILLER, M.D., obstetrician and gynecologist, brother of the late Dr. C. Jeff Miller, died April 20, 1945, at his home in New Orleans, Louisiana, of heart failure, at the age of 52 years. Born in Winchester, Tennessee, Sept. 25, 1893, he took his medical degree at Tulane University and served internships at the Charity Hospital, New Orleans, and the New York Lying-In Hospital. He entered the Medical Corps of the Army during World War I as first lieutenant. On his return to civil life he became instructor in obstetrics and gynecology at Tulane until 1924, then assistant professor until 1936, and then professor and head of the department until his retirement a year ago.

Dr. Miller was a member of his State and National Societies, The American College of Surgeons, The American Gynecological Society, Gynecological Travel Club (President), Southern Medical Association, New Orleans Obstetrical Society, and others.

Correspondence

Continuous Caudal Analgesia

To the Editor:

In the Dec. 30, 1944, issue of the *Journal of the American Medical Association*, Dr. Robert A. Hingson gives an interim report on caudal analgesia from a number of clinics. In it there are the following statements:

"This study compares so favorably with all other forms of pain relief in obstetrics that its significance is self-evident; the fetal mortality in this group has been 1.7 per cent as compared with the fetal mortality in the death registration area of the United States of 5.2 per cent. Out of these 42,000 cases there have been sixteen maternal deaths. Six were attributed to obstetric complications, seven to the misuse of caudal analgesia in unskilled hands and three may be considered anesthetic deaths—emphasizing the small permanent hazard to the mother associated with this form of pain relief."

Only six maternal deaths due to obstetric complications out of 42,000 cases is an amazingly low mortality, and should be elucidated as to how caudal analgesia produced that result. Why should there be three anesthetic deaths if the women had caudal analgesia? Seven women did lose their lives due to caudal analgesia, and how many more paid the penalty in other institutions whose deaths were not publicized?

The 5.2 per cent fetal mortality is the gross uncorrected mortality rate from all sections of the United States not only from the large clinics. Is the 1.7 per cent fetal mortality in this series also the gross uncorrected mortality or is it the mortality attributed to labor and delivery only? The comparison should be made for each institution between the caudal series and the other methods of analgesia and anesthesia.

"Parturients in whom fear can be controlled by confidence in their physician and in their surroundings are the ideal ones for the use of continuous caudal and spinal analgesia."

This class of patients does not need caudal analgesia, all they need is some morphine to ease the pain of the first stage of labor and ether at the time of delivery.

"Parturients in whom fear is uncontrolled can still be more satisfactorily managed with amnesia and general anesthesia."

If that is the case, then caudal analgesia loses all its attraction, for it is the nervous, hysterical and temperamental woman in labor that we are searching for a means to quiet. If we cannot use it on her, then the level-headed type does not need caudal analgesia and should not be subjected to it.

MORRIS LEFF, M.D.

NEW YORK, N. Y.

JANUARY 10, 1945.

Reply by Dr. Hingson

To the Editor:

The paper published as an interim report on caudal analgesia by me in the Dec. 30, 1944, issue of the *Journal of the American Medical Association* is at present out of date by recent experience, since this paper includes only an analysis of cases up to May 1, 1944.

Already 50,000 deliveries under continuous caudal analgesia have been reported to the Graduate Medical Course of the Philadelphia Lying-in Hospital by physicians who have completed the course and by physicians who have managed large groups of cases without training. In this compilation, there have been 19 maternal deaths which will be adequately considered in a forthcoming scientific paper to the profession. The comparison of fetal mortality from all sections of the United States with the fetal mortality in this reported series was made under identical conditions. It is the gross and uncorrected fetal mortality for both groups, which include hospital and nonhospital deliveries from all sections of the Country.

The last two questions raised may be answered by pointing out that Dr. Leff has not considered the welfare of the baby in either question. The day is past when women in labor are managed with morphine and ether without regard to their welfare. We now recognize the dual responsibility of selecting the form of management for the patient that is most satisfactory and the safest for her and her newborn baby.

ROBERT A. HINGSON, Surgeon
U. S. Public Health Service.

JANUARY 15, 1945.

Items

American Board of Obstetrics and Gynecology

Examinations

The general oral and pathology examinations (Part II) for all candidates will be conducted at Atlantic City, New Jersey, by the entire Board from Wednesday, June 13, through Tuesday, June 19, 1945. The Hotel Shelburne in Atlantic City will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel.

Candidates for *re-examination* in Part II must make written application to the Secretary's Office not later than April 15, 1945.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

Deferment without time penalty under a waiver of our published regulations applying to civilian candidates, will be granted if a candidate in Service finds it impossible to proceed with the examinations of the Board.

Applications are now being received for the 1946 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

Announcement

In compliance with the directives imposed by the War Production Board limiting the amount of paper consumed in the production of this JOURNAL, the publishers find it necessary to change the format. As soon as these restrictions are lifted the original format will be restored. Even though the number of pages has been reduced, the actual content of the JOURNAL has not been decreased to any appreciable extent.

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Original Communications

ESTIMATION OF THE WORK OF OBSTETRIC LABOR AND ITS SIGNIFICANCE IN HEART DISEASE

MAJOR JOHN J. SAMPSON, M.C., A.U.S., ELISE M. ROSE, M.D., AND
ROBERT QUINN, LIEUTENANT (S.G.) (MC), USNR, SAN FRANCISCO, CALIF.

(From the Departments of Medicine and Obstetrics, University of California)

IT MAY be assumed that both pregnancy and labor are accompanied by increased cardiac effort. The degree of this increment varies widely in different cases, either with or without complications. It is the purpose of this paper to present an estimate of the amount and character of physical effort during labor, especially as it induces increased cardiac work. There is considerable difference of opinion as to the magnitude of the work involved in labor, especially regarding the possibility of precipitating heart failure in cardiac patients.

It is recognized by many clinicians that a cardiac patient in Class II or Class III (moderate or severe heart failure, American Heart Association Classification) is likely to have prolonged or permanent reduction of her cardiac reserve after a single episode of excessive physical work. With voluntary effort, the protective mechanism, as dyspnea, will generally force the patient to stop such effort prior to precipitation of serious heart failure. In labor much of the work done is involuntary and, therefore, not subject to control even though protective and warning signs and symptoms develop. It would, therefore, seem reasonable to protect such patients against excessive loads of work by early termination of pregnancy, or cesarean section if it could be shown that the work was of the magnitude commonly recognized as capable of producing serious heart failure, or permanent reduction of cardiac reserve. Although Boyer & Nadas¹ recently showed that life expectancy was not shortened by pregnancies, in a statistical survey of one hundred and three cardiac patients, experience with individual cases, such as Case 41 in this series, suggests reduction of cardiac function may follow obstetric labor.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Although one cannot with certainty predict that a Class I or mild Class II patient may not develop more serious failure late in pregnancy, the attendance of clinicians in obstetric clinics to evaluate for the obstetrician the gravity of heart disease in pregnant women, has resulted in a lowered fatality of cardiac cases. The skillful care given to patients bordering on failure is as much responsible for this lowered fatality rate as the early interruption of pregnancy in women who were poor obstetric risks.

Thus, with the establishment of cardiac obstetric clinics, many hospitals have reported no cardiac obstetric fatalities for several years. However, it is recognized that an irreducible minimum of cardiac deaths may occur. This has been given by Hamilton and Thomson² as 2.5 per cent and constitutes the following complications: Embolism, bacterial endocarditis, sepsis, and hemorrhage. Of these, bacterial endocarditis is the only true cardiac complication, and it constitutes only 0.75 per cent of cardiac deaths during pregnancy. Hamilton has rather arbitrarily divided his series of cases which total 894 into a favorable and unfavorable group. Those in the unfavorable group have had signs or history of heart failure, auricular fibrillation, or have had serious complicating diseases. The mortality is 16 per cent for his series of unfavorable patients. He gives a mortality of 33½ per cent for patients with auricular fibrillation. In the favorable group, Hamilton and Thomson have reported over 320 consecutive cases, during one period of their study, without loss of a patient from congestive heart failure.

TABLE I. OBSTETRICAL CARDIAC CASES OBSERVED—MAY, 1936 THROUGH OCTOBER, 1942, UNIVERSITY OF CALIFORNIA HOSPITAL

TOTAL CLINIC DELIVERIES—3,180		ORGANIC HEART DISEASE*—80	
PERCENTAGE CARDIAC—2.5			
NO MATERNAL OR TERM FETAL DEATHS IN CARDIAC CASES			
ETIOLOGY AND TYPES OF LESIONS			
<i>Rheumatic</i> —57		<i>Congenital</i> —14	
Mitral insufficiency	20	I-V Septal Defect (1 Compl.	6
Mitral insufficiency and stenosis	32	A-V Block)	2
Aortic insufficiency, mitral		Aortic coarctation	2
insufficiency and stenosis	5	Subaortic stenosis	1
<i>Doubtful Rheumatic</i>		Patent ductus arteriosus	2
Mitral insufficiency	3	Pulmonary stenosis (1 Tetral. of	3
		Fallot)	1
<i>Thyrotoxic</i>	4	<i>Hypertensive-Coronary Arteriosclerosis</i>	1
		<i>Beriberi</i>	1
ARRHYTHMIAS			
Ectopic beats	4	Complete A-V heart block	1
Paroxysmal tachycardia	7	Auricular fibrillation	2
COMPLICATIONS			
Bronchitis and pneumonia	3	Acute rheumatic fever	1
Pulmonary infarct	2	Subacute bacterial endocarditis	1
		(Mother lived 5 months post partum)	
		Normal child	
CLASS OF CARDIAC FUNCTION			
I—17	II (IIa)—46	III (IIb)—15	IV—0
Unclassified—2			
MODE OF DELIVERY			
Abortions, miscarriages, hysterotomies	5	(3 group III)	Midforceps Cesarean cardiac indication Cesarean obstetric indication Undelivered as of October 15, 1942
			1 (group III) 3 (group III) 11 4
Spontaneous	39	(5 group III)	
Low forceps	18	(3 group III)	

*This includes 2 successive deliveries on each of 5 patients.

At the University of California Hospital, there have been 90 cardiac obstetric patients cared for within the six years of 1936 through 1942, without death from any cause. The diagnostic classification (American Heart Association Classification), complications, and mode of delivery of 89 per cent of these patients are given in Table I. Undoubtedly, there will be fatalities from one or another of the "irreducible minimum" causes of fatality as future cases are added to the series.

It is a belief, well substantiated statistically, that rheumatic heart disease patients tolerate surgery well and, therefore, should tolerate cesarean section. The death of approximately 50 per cent of all cardiac obstetric fatalities occurs within the first forty-eight hours after delivery according to Hoffman and Jeffers³ including the cesarean sections. It is assumed that certain changes occur in the maternal circulation after delivery which may precipitate heart failure, and investigation of these changes is now being undertaken by the personnel at the University of California Obstetrical Cardiac Clinic. Even if some of these postpartum changes occur after cesarean section, such mode of delivery may be indicated, if it can be shown that the work of labor may be of significant magnitude and that in any particular case, it may be unpredictable. The operative and postoperative risk of this procedure must naturally be weighed against such prospective reduction of the cardiac hazard.

There have been reported recently, certain circulatory changes which may place an increasing burden on the heart as pregnancy advances. These changes have led to the conclusion by Hamilton and Thomson,⁴ that if a patient be carried through the eighth lunar month, she should then be permitted to complete her term of pregnancy. Failure is less likely to occur in the ninth and tenth months than in the eighth month according to Cohen and Thomson.⁵ Cohen and Thomson⁵ (Fig.1) and Burwell⁶ are largely responsible for the following information: There is an increase of (1) blood volume to a maximum of about 45 per cent; (2) of cardiac output to a maximum of about 50 per cent; (3) of the oxygen consumption or metabolic rate to a maximum of 15 to 20 per cent; and (4) there is a decrease of the arteriovenous oxygen difference, presumably due to shunting through the placenta. Although, as stated, these changes start about the fifth month and reach their peak at 8½ months, the presumed increments of unavoidable work are still elevated at term, and therefore, are a burden added to that of labor.

Hamilton and Thomson² report a maternal mortality of 8.3 per cent on cesarean section cases as against 2 per cent by pelvic delivery, with 5 per cent mortality from heart failure in the former group, and 7 per cent in the latter group. They make no comment on the degree of heart failure in the patients selected for cesarean section, but the high fatality rate in this group may have been due to the selection of patients with more serious heart failure.

Harrison⁷ has shown that cardiac patients develop greater oxygen debts than normal individuals only after extreme physical effort that approaches their maximum capacity. Dyspnea ordinarily checks the amount of work done, but it can be readily seen that with obstetric labor this work undertaken is often impossible to control, and may seriously tax the limited circulatory capacity of a cardiac patient. Dyspnea here can be no check and the result may be serious. The

capacity to supply oxygen to the tissues is limited. It may approach twenty times the basal metabolic rate in an athlete, and it is known that training improves the coefficient of utilization of oxygen and throws less work on the heart. In cardiac patients, the coefficient of utilization or the amount of oxygen taken up per unit of blood may be normal, but their training is generally poor and therefore, we would expect this factor to be low.

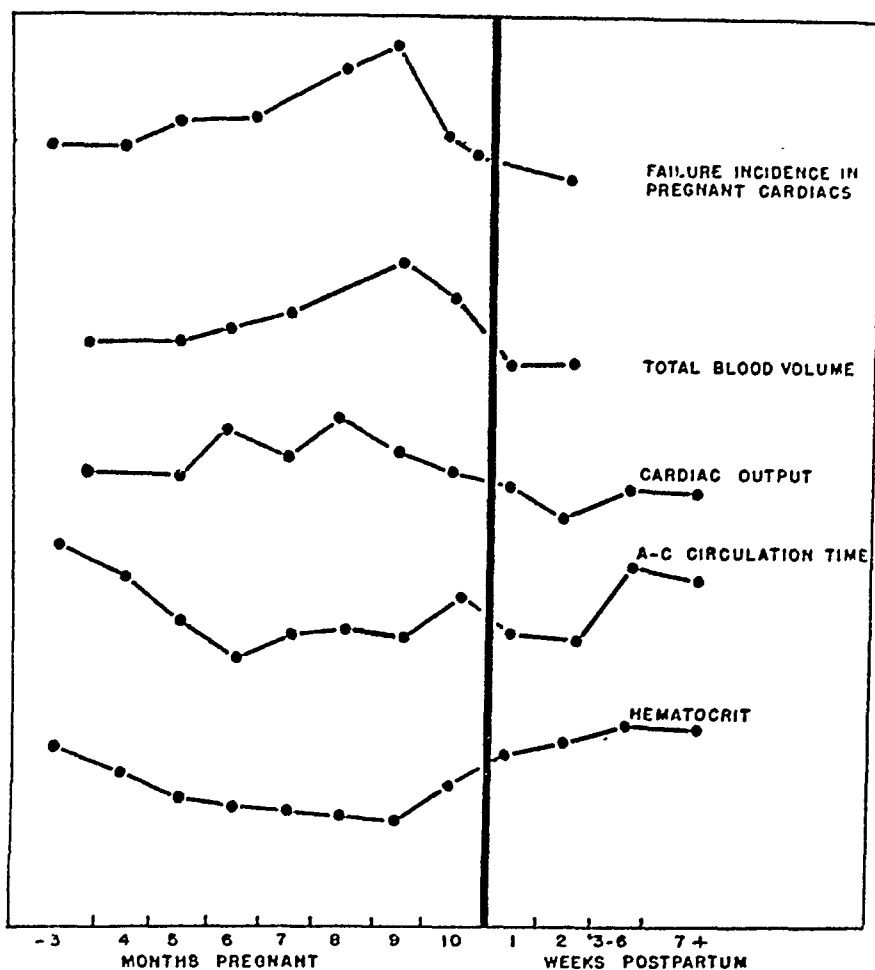


Fig. 1.—Circulatory burden on the heart in pregnancy. (From Cohen and Thomson, *J. A. M. A.* 112: 116, 1939.)

There has been recently an effort to measure the amount of work during the first stage of labor by Woodbury, Hamilton and Torpin.⁸ By the use of manometers connected to the brachial artery, the duodenum, and the fundus of the uterus they estimated the differential pressures in the abdomen, in the uterus, and in the maternal placental blood vessels. They estimated that 25 to 95 mm. Hg pressure was present in the uterus with each pain, and that a maximum of 500 grams pressure per square cm. cross section of the uterine wall occurred. Their most interesting conclusion was that the bearing down forces of the abdominal and chest muscles were not expulsive before cervical dilatation, but materially diminished the maternal placental blood pressure even to the zero point. These forces, however, were effective in expulsion of the fetus after cervical dilatation. Such anesthetics and hypnotics as morphine sulfate, barbiturates, nitrous oxide and oxygen, and cyclopropane diminished these extrauterine forces and actually increased the maternal placental arterial blood pressure. Epinephrine likewise, increased that blood pressure and as such, diminished the chances of fetal anoxia.

In 1936, Stahler⁹ published an article entitled "The Physiology of Work in Pregnancy." Although this paper included a section describing the changes in character, rate and depth of respiration during

labor, and a section on the physiology of work during pregnancy, the section of chief interest to us was that on the measurement of work in labor. He measured the oxygen consumption and carbon-dioxide output for a short period in the first or early stage of labor, during the expulsive period, and in the immediate postpartum period. His estimation of the gas exchange for the entire period of labor was based on a summation of the single observations made during each of three or four stages, and assumed that this represented the average figures for the whole individual stage studied. He then converted his increment in gaseous exchange into calories, and estimated that the work of delivery varied from 166 to 1,555 calories. He estimated that the work of an average 16-hour primiparous delivery was the equivalent of two hours' heavy work of a stonemason or woodcutter. The patient with the greatest energy consumption was estimated to have done the work equivalent to a 30-kilometer march on the level. The average caloric expenditure was 42 calories per hour, and the maximum 56 calories per hour during the pushing efforts. Lusk¹⁰ estimated the calories of work at 214 per hour for a laundress at work, and 378 per hour for a man sawing wood.

We have found that such spot determinations in the three or four phases of labor made by Stahler⁹ do not give an accurate picture of the total oxygen consumption or the periodic character of the work undertaken. Whereas, as will be shown, our estimates of total work done in labor are of the same order as those of Stahler,⁹ different conclusions will be placed on the magnitude of cardiac strain or demands involved. Likewise, we have observed great variation in respiratory rate and depth with the voluntary and involuntary work. Another observation on the respiration in our cases was that after a period of hyperpnea, there was a leveling off of the curve of oxygen consumption. This was probably due to absorption of the increased alveolar oxygen content and was succeeded by a uniform progress of the line of oxygen uptake.

Technique

Forty-two patients were studied during obstetric labor. Three cases were excluded from the tabulation (Table II) because the recordings were insufficient to draw any satisfactory conclusions. On ten cases oxygen intake was measured in selected periods of over six minutes each at various times during the first three stages of labor, and through the first two hours of the postpartum period. In 29 cases only the postpartum oxygen consumption was measured. The ordinary Roth-Benedict type of metabolism apparatus was used with the standard rubber mouthpiece. The oxygen utilization as well as the depth and rate of respiration were recorded on the kymograph.

The measurement of oxygen utilized was accomplished by plotting graphically the oxygen consumption in cubic centimeters per minute for each determination and connecting by line the midpoint of each determination to form an angular graph. The area under the curve obtained by connecting these points using the basal metabolic rate as the base line was then obtained by use of a planimeter. Technical differences in obtaining determinations on patients during labor with struggling, vomiting, fatigue, or short periods of gas anesthesia interfered with certain of the tests made, but generally satisfactory curves could be obtained.

In certain cases continuous readings were obtained during the entire postpartum period. Since the plotted graphs of continuous oxygen uptake did not materially differ from those in which the patient was allowed short rest periods of 1 to 10 minutes breathing atmospheric

TABLE II. DURATION OF EXCESS OXYGEN CONSUMPTION AFTER DELIVERY IN 39 PATIENTS

<i>Primipara: (15 Uncomplicated)</i>	
2—	Oxygen consumption returned to basal level within $\frac{1}{2}$ to $\frac{3}{4}$ hour after delivery
2—	Oxygen consumption returned to basal level within $\frac{3}{4}$ to 1 hour after delivery
11—	Oxygen consumption did not return to basal level until after 1 hour after delivery (6 showed "oxygen debt" at conclusion of observation period)
<i>Multipara: (16 Uncomplicated)</i>	
1—	Oxygen consumption returned to basal level under $\frac{1}{2}$ hour after delivery
2—	Oxygen consumption returned to basal level within $\frac{1}{2}$ to $\frac{3}{4}$ hour after delivery
5—	Oxygen consumption returned to basal level within $\frac{3}{4}$ to 1 hour after delivery
8—	Oxygen consumption did not return to basal level until after 1 hour after delivery (4 showed appreciable "oxygen debt" at conclusion of observation period)
<i>5 Rheumatic Heart Disease Cases:</i>	
<i>2 Cases—Class II</i>	
	Both were multipara and oxygen consumption returned to basal levels under 1 hour
<i>3 Cases—Class III</i>	
1—	(Primipara). Delivered by cesarean section—first stage—oxygen consumption returned to basal level immediately after delivery
1—	(Multipara). 18% excess oxygen consumption at $1\frac{1}{2}$ hours after delivery
1—	(Primipara). 20% excess oxygen consumption at 2 hours and 25% excess oxygen consumption at 2 days after delivery
<i>3 Cases: (Complicated)</i>	
Case 17:	(Multipara)—57% excess oxygen consumption in 1 hour 10 minutes after delivery. Large baby—moderate dystocia
Case 18:	(Multipara)—Thyrotoxic—oxygen consumption excess and increasing 1 hour after delivery, over basal figures determined 2 weeks post partum
Case 42:	(Multipara)—Breech presentation—37% oxygen consumption excess over basal level 2 hours after delivery

air, it was assumed that little difference was made in estimation of total oxygen absorption by such breaks in the curve. Therefore, all later curves were made in broken periods. Gagge¹¹ has used this technique effectively in measuring similar periods of oxygen consumption.

Although it is not entirely essential in these case studies, for the purpose of comparison with common daily forms of physical work the oxygen consumed can be approximately translated into terms of kilogram-meters of work or calories of heat produced. Assuming basal fasting conditions, Shock's¹² ratios of 2 c.c. to 4 c.c. O_2 consumed per kilogram-meters of work and Lusk's¹³ ratios 4.825 of calories per liter of oxygen have been used in Table III.

It is impossible to translate exactly the amount of oxygen utilized into kilogram-meters of work for the following reasons:

1. As has been shown by Shock¹² and others, the efficiency of work done varies inversely with the rate at which it is performed. Thus, in stair climbing measurements on adolescent girls, Shock¹² found that in their climbing $4\pm$ cubic centimeters of oxygen were utilized to each kilogram-meter of work when that work was done within two minutes; whereas, only $2\pm$ cubic centimeters of oxygen were used when that work was accomplished in over $3\frac{1}{2}$ minutes.

2. The development of an oxygen debt, as shown by Margaria and Edwards,¹⁴ is dependent not only on the excess oxygen needed for the increased muscular work, but also approximately one-third of the total oxygen debt developed is due to an increase of the general tissue metabolism over the resting level, probably due to thyroid or other endocrine stimulation.

3. It is recognized by Hill and Flack,¹⁵ and others that breathing oxygen improves the efficiency of the circulation during work, and likewise that there is probably some reduction in the amount of oxygen debt accumulated during work when oxygen is inhaled.

Results

The duration of significantly increased oxygen consumption over basal levels in 39 cases is given in Table II. Although persistent in-

TABLE III

CASE NO.	AGE	PRIMI- PARA MULTI- PARA	CL. DIAGNOSIS FUNCT. CLASS.	TYPE DE- LIVERY	DURATION FIRST STAGE	DURATION SECOND STAGE	CHAR. PAINS SECOND STAGE	POST DELIVERY MEDICATION	EPI- OP- ONY
39 K	22	Primipara	Nervous Tension Hyperventilation	Low Forceps ROA	16 hours 10 minutes	95 minutes	Poor—Fair No expul- sions Pains	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c.	Yes
40 P	28	Primipara	Mitral stenosis and Insufficiency Auricular fibrilla- tion Class IV	Low Forceps LOA	4 hours	39 minutes	Fair	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c.	Yes
41 W	32	Multipara Para vi	Normal	Spont. ROA OA	4 hours 45 minutes	13 minutes	Fair to Good	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c. + 1 c.c. pit.	Yes
42 R	22	Multipara Para ii	Normal	Breech Spont.	15 hours 32 minutes	20 minutes	Fair to Good	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c.	Yes
43 V	38	Multipara Para viii	Mitral stenosis and Insufficiency Hyperventilation Class II-III	LOA Spont.	2 hours 40 minutes	17 minutes	Poor at first Good last 1½ hour	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c. Cod. and Aspirin	No
44 A	34	Multipara Para iv	Normal	LOA Spont.	6 hours 10 minutes	5 minutes	Rapid 2nd Stage Forceful	Baserg. 1 c.c. Neogyn. 2 tab. Ergot. 1 c.c.	No

(Continued on next page)

TABLE III.—CONT'D

TOTAL ESTIMATED OXYGEN INTAKE OVER BASAL CONSUMP- TION	WORK ESTIMATED		OXYGEN CONSUMPTION RETURNED TO APPROXIMATE BASAL LEVELS		
	IN KG./M.	IN CALORIES	UNDER 1 HOUR	OVER 1 HOUR	% OVER AVERAGE BASAL AT TIME OF LAST DETERMINATION
60,560 c.c.	15,140 minimum 30,280 maximum	297		+	0 1 hour 5 minutes
34,650 c.c.	8,662 minimum 17,325 maximum	167		+	25% + on 2nd day
20,400 c.c.	5,100 minimum 10,200 maximum	98.43	+		0 1 hour 9 minutes
55,290 c.c.	13,822 minimum 27,645 maximum	266		+	37%—2 hours
23,720 c.c.	5,930 minimum 11,860 maximum	114		+	18.7% 1 hour 34 minutes
20,304 c.c.	5,085 minimum 10,170 maximum	100—	+		0

Note: Using the ratio of 0.4268 Kg./M. to 1 calory and estimating that approximately 25% of the heat production represents work, the resultant figures for Kg./meters approximates very closely the maximum conversion ratio furnished by Shock¹², namely, 2 c.c. \pm oxygen consumption represents 1 Kg./M. of work as given in this table.

crease of metabolic demands could account for the excess oxygen consumption, the relatively rapid return to normal suggests that the excess oxygen intake represents repayment of oxygen debt incurred by the work of labor. The delayed return to basal levels probably represents a greater debt or faulty cardiorespiratory mechanisms.

In an analysis of the fifteen uncomplicated primiparas studied, it will be seen that eleven (73 per cent) did not dispose of their oxygen debt until after 1 hour, in contrast to eight (50 per cent) of the sixteen uncomplicated multiparas.

Basal oxygen consumption determined 2 to 14 days before labor differed from that determined on the fifth to the twentieth day after labor, by rates varying from 20 per cent lower to approximately the same rate. The majority of cases showed about 10 per cent lower basal oxygen consumption after delivery than before labor. It has not been determined when this postpartum fall in metabolic rate occurs. Likewise, the cause of elevated rate in pregnancy is not known although probably accounted for in part by the fetal metabolism. Several patients fell to a subbasal level at 1 to 2 hour post partum, especially when fatigued and sedated, and some of these patients actually fell asleep while the postpartum oxygen determination was being made.

Since it was impossible to predict the patient, who temperamentally would prove a suitable subject for study, and since the differences of antepartum and postpartum basal metabolic rates as measured on the first twenty-nine cases were so little, only postpartum basal oxygen consumption was measured in the last 13 cases. In only one instance was an abnormally high metabolic rate obtained; this in a woman with a mild hyperthyroidism due to administration of 1 gr. of thyroid extract (Armour) per day, during her entire pregnancy. The results of the oxygen studies in this patient were not possible to evaluate as thyroid substance was not administered post partum and therefore, the increment of oxygen consumption during labor could not be compared to the estimated basal rate at that time. None of the group was fed during labor. In the six patients with the most complete observations through all stages of labor (Table III), the specific dynamic action of food may probably be disregarded since none had been fed for about five hours before the second stage of labor. Therefore, the metabolic rate would probably not be elevated from this source over 5 to 10 per cent of the recorded basal oxygen consumption during the later stages of labor.

The characteristic curve, especially in the postpartum period of the uncomplicated primiparous patient is illustrated in Fig. 2, Case 39. This curve does not show studies immediately before delivery, and commonly in primipara, there was moderately but not greatly elevated oxygen consumption at this time. Immediately following delivery, there is generally a flattened curve with the return to basal levels delayed longer than in the multiparous patients. A similar curve of postpartum period is seen in Fig. 3, Case 25. The antepartum oxygen determinations illustrate the fluctuation that often occurs—increasing

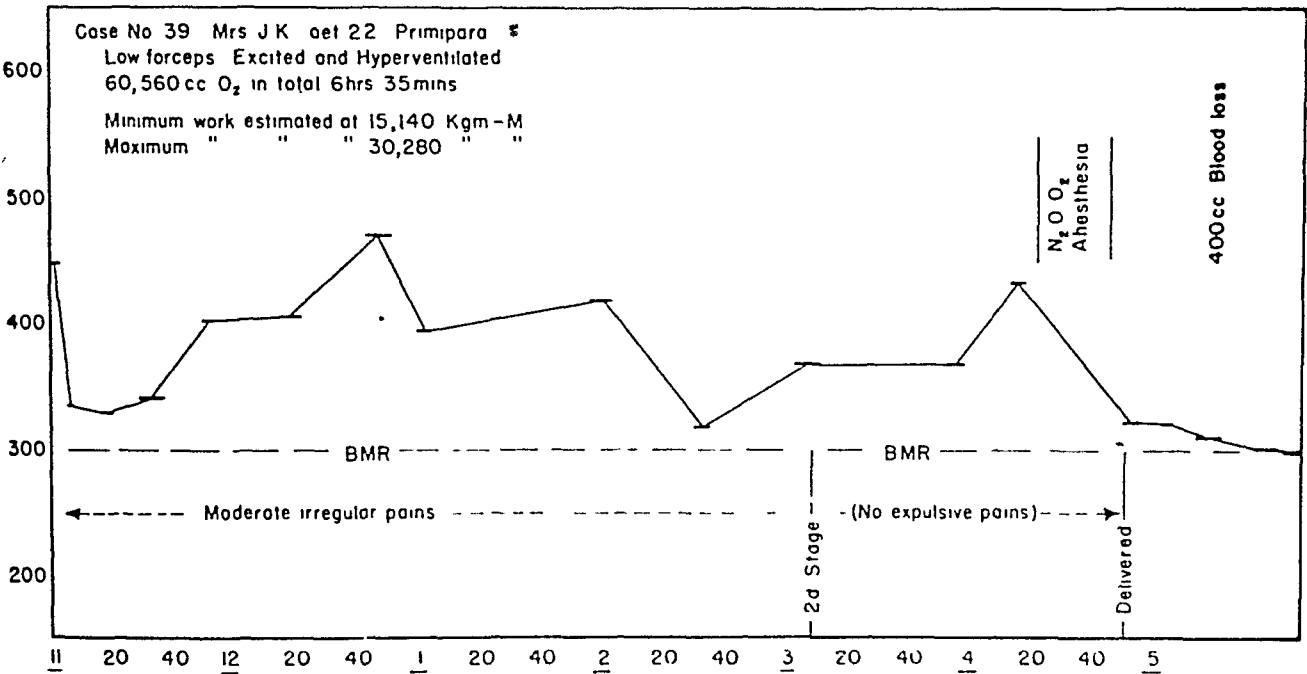


Fig. 2.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time. This applies also to Figs. 3 to 8.

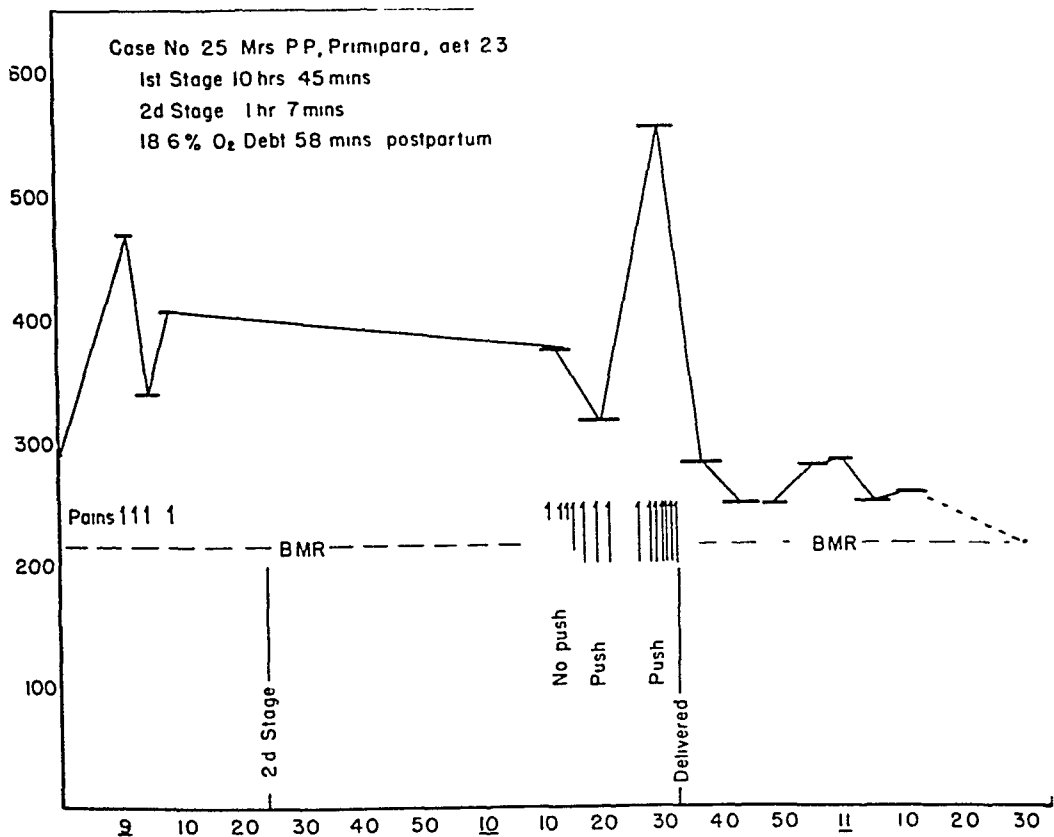


Fig. 3.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

with periods of actual pains and returning to near basal levels when quiet (Case 39). The first oxygen determinations in this patient (Case 39) may be disregarded, having been made shortly after walking into the hospital. This was an excitable, restless patient, and some of the early fluctuations may have been exaggerated by muscular activity. She used little voluntary effort, and low forceps were applied for delivery.

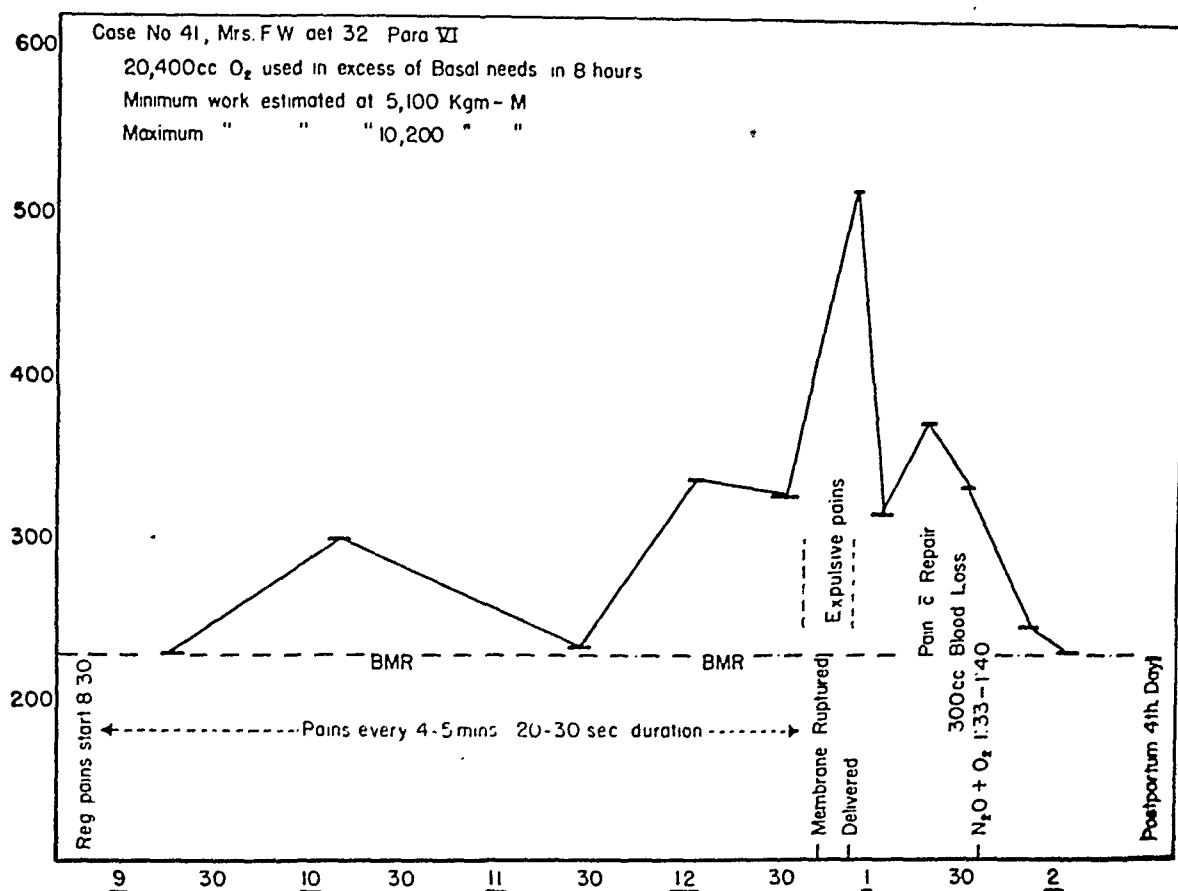


Fig. 4.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

The most characteristic curve of multiparous patients is illustrated in Fig. 4, Case 41. There is a relatively late, steep rise of the curve, often 100 per cent to 400 per cent of the basal level. There is then a rapid drop with a secondary rise and a prompt return to basal levels. The initial fall of oxygen consumption immediately after delivery may be due to overventilation. This type of curve in many multiparous patients resembles the character of curves obtained in normal human beings after any sudden violent effort such as running. Fig. 5, Case 43, illustrates a high and abrupt rise of oxygen consumption that occasionally occurs as an exaggerated form of the previous curve probably resulting from a psychic tachypnea, although this patient had asymptomatic mitral valvulitis. Likewise, Case 42, Fig. 6, a breech presentation, serves to illustrate that form.

In the patients with rheumatic heart disease, there were five cases, all with mitral stenosis and insufficiency (Table II). Two classified as Group III were multiparous, and returned to their basal rate under one hour, illustrating the benign type of cardiac patient who does not require special obstetric procedure.

All of the three cases grouped in Class III, had shown various degrees of heart failure during pregnancy.

Case 43, Fig. 5, was a multipara who had developed marked dyspnea on effort in the last three weeks of her pregnancy. She showed evidence of failure during expulsive pains immediately preceding delivery. Her respiratory rate was maintained at 45 per minute for approxi-

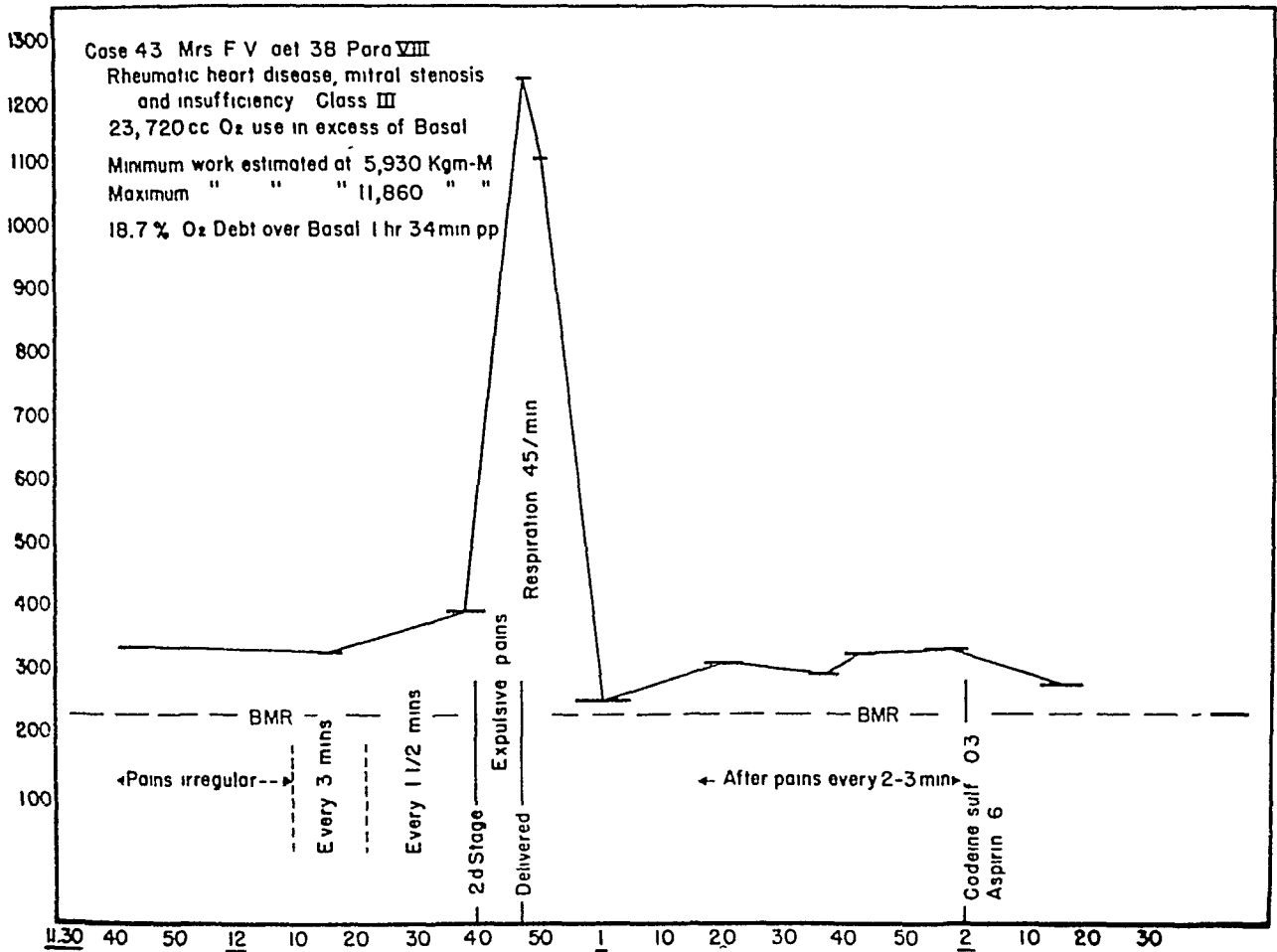


Fig. 5.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

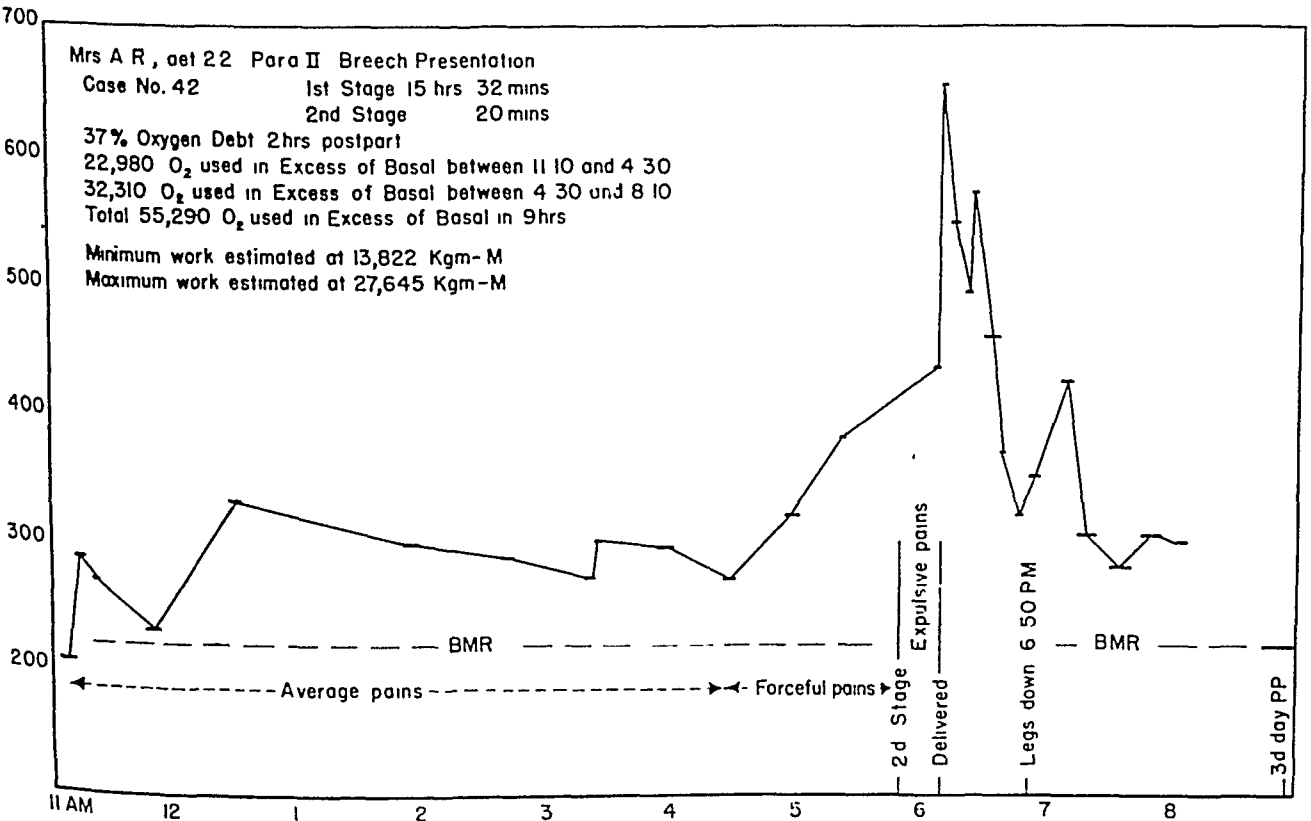


Fig. 6.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

mately 15 minutes, and there was a tremendous increment of oxygen utilization. She showed an 18 per cent "oxygen debt" 11½ hours after delivery, but there was an abrupt return to low levels of oxygen intake after the period of high consumption. She presented no signs of heart failure after delivery.

Case 24, Fig. 7, was a 30-year-old woman in her second pregnancy, the first having terminated in a spontaneous abortion in the fourth month. She had increasing signs of congestive heart failure and a

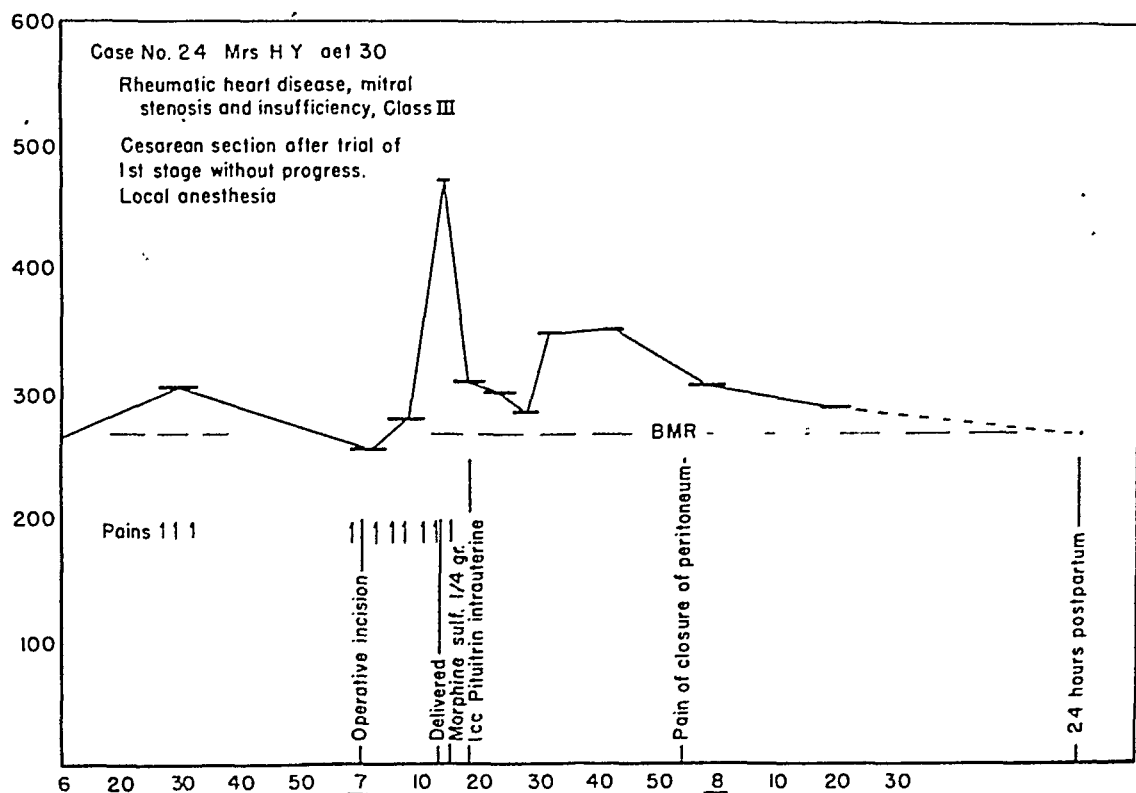


Fig. 7.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

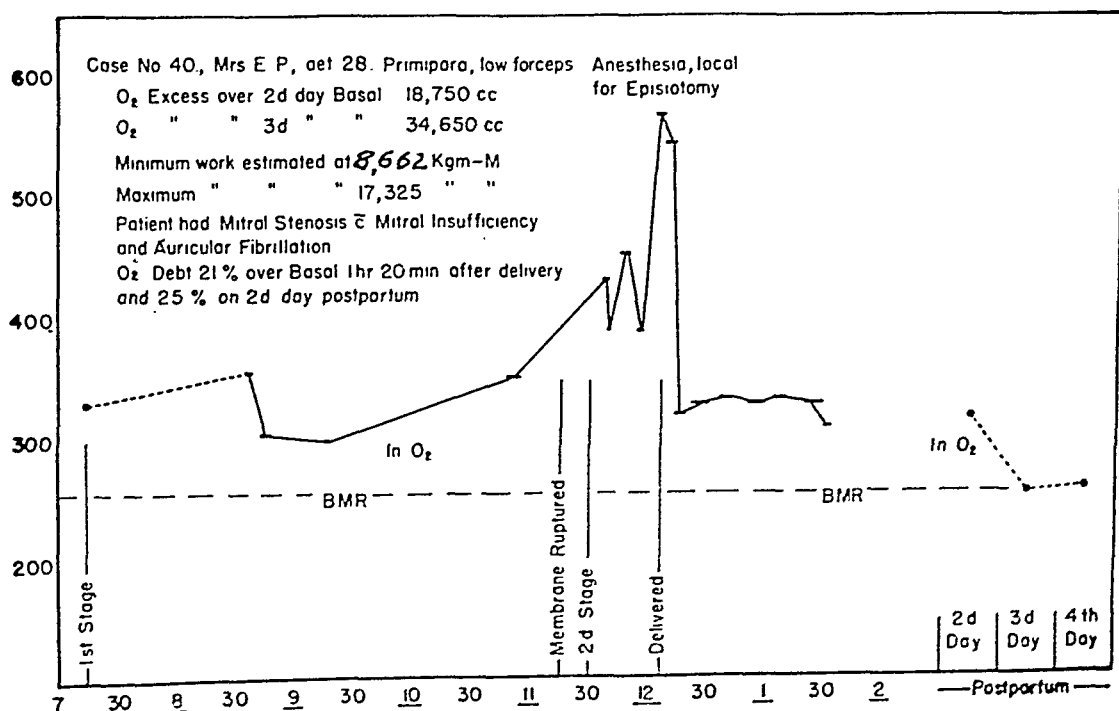


Fig. 8.—Numbers at side denote oxygen consumed per minute-cubic centimeters, at bottom the time.

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cesarean section was accomplished at term with uneventful recovery. Fig. 7 is a graphic record of the oxygen consumption determined through the operation. She was having mild first-stage labor pains at the time, having made no progress with labor in thirteen hours. With exception of the transient rise during manipulation of the uterus and the somewhat more prolonged rise after intrauterine pituitrin, there was little excess oxygen utilized. An increased oxygen consumption following pituitrin administration intramuscularly was observed in this as in many of the patients delivered vaginally.

Mrs P. (Primipara) Rheumatic Mitral Stenosis and Insufficiency Auricular Fibrillation
8/27/41

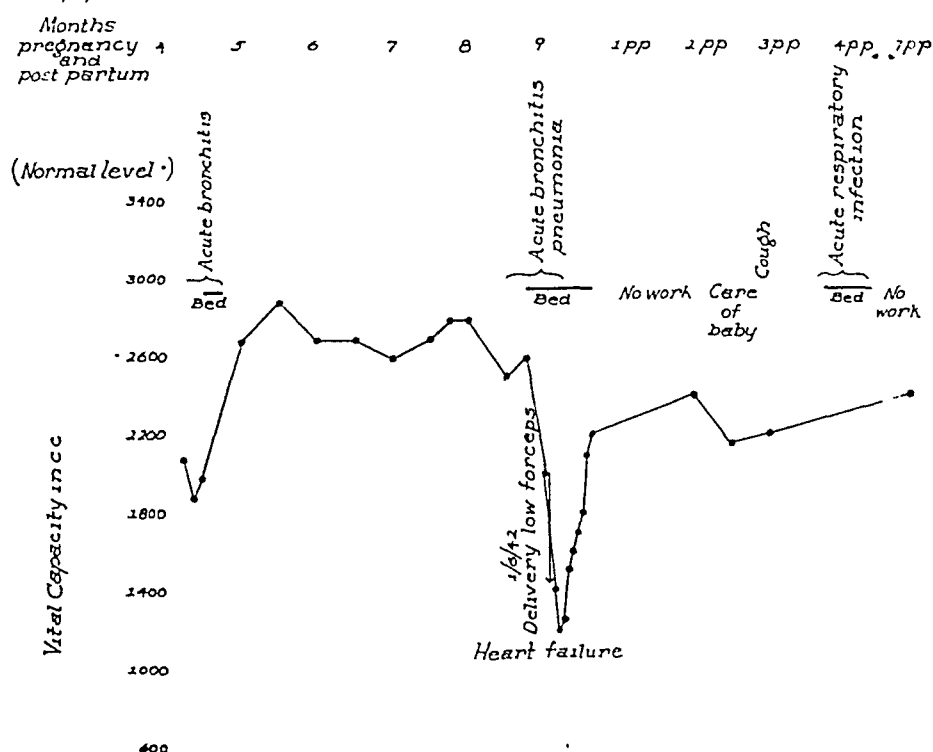


Fig. 9.—Vital capacity in complicated cardiac pregnancy.

Case 40, Fig. 8, was that of a primiparous woman, aged 28 years, with mitral stenosis and insufficiency, auricular fibrillation with moderate congestive heart failure and under constant digitalis therapy. Succeeding an attack of acute bronchitis in the fourth month of pregnancy, she was confined to rest at home. During the ninth month of pregnancy, her dyspnea increased and she was hospitalized, and developed another acute respiratory tract infection at term. Elevated venous pressure and pulmonary râles developed in the last two hours of labor and she was given oxygen continuously, not only for measurement of her oxygen intake, but also for the therapeutic effect. The forceful labor pains lasted about 2 hours, 40 minutes of which were occupied with severe expulsive contractions. She was discouraged from voluntary effort.

The oxygen consumption fell rapidly after delivery by low forceps, but remained constantly elevated at between 20 and 25 per cent above the basal level for the succeeding hour and a half, and through the next 36 hours. An isolated determination 11½ hours after delivery showed a marked elevation following excitement. This patient's vital capacity changes are shown in Fig. 9, and illustrate the rapid fall with the respiratory tract infection and the recovery which covers a period of about four weeks. At no time had the vital capacity recovered the antepartum level in the next seven months, which indicates that the functional damage to the heart following the pregnancy, labor, and respiratory tract infection was probably permanent.

Three cases of complicated labor were studied, all multiparous.

Case 17 had a long difficult labor with a large baby, and showed a 5 per cent "oxygen debt" one hour, ten minutes post partum.

Case 18, a thyrotoxicosis, showed a continuous rising curve of oxygen utilization for one hour after delivery, and probably illustrates the effect of labor in increasing the basal metabolic rate.

When any complication in labor develops which interferes with prompt delivery or increases the work of delivery, even in multiparous women, the oxygen consumption curve reflects the degree and often the pattern of the time distribution of this work. This is illustrated in Fig. 6, Case 42, of a multiparous woman with a breech presentation. In this patient, there was a slightly greater oxygen intake through the early first stage and a progressive increase with the onset of forceful pains prior to, and through complete cervical dilatation.

There is no indication that the work pattern follows the arbitrary division into first and second stages of labor. The peak immediately after delivery was followed by a prompt drop and a secondary rise, as was often found in our series of cases. There was then a delay in the return to the basal levels suggesting a persistent oxygen debt and, therefore, a load of work not readily compensated for by the normal respiratory and circulatory mechanisms of this woman. The graphic illustration of this type of response serves to show that even a multiparous woman may have a high work increment during labor.

In addition to these three cases, two of the primiparous cases presented slow returns to the basal level having relatively prolonged and more severe labors with "occiput posterior" presentations.

In the six instances of forcep applications in our series, no undue oxygen demand was evidenced.

The use of chest and abdominal muscles in forceful and voluntary pushing resulted in an abrupt increase of the oxygen intake as illustrated in Fig. 3, Case 25. This may represent a possible danger to the cardiac patients, and proposes the question as to whether this type of effort, either voluntary or involuntary, will cause more harm to the patient than the prolongation of a less strenuous labor as by use of anesthesia.

The estimates of oxygen consumption in these 6 cases studied through all stages of labor varied from 20,400 c.c. in an uncompleted multiparous patient with $4\frac{3}{4}$ hours of first stage, and 13 minutes second stage of labor to 60,560 c.c. in a primipara with approximately 16 hours of first stage, and 1 hour second stage. Using the basal factor of conversion ratio of 4.825 Cal. per liter of oxygen, these figures are somewhat less than Stahler's figures, namely, 96.5 to 292 Cal. as contrasted to 166 to 1,555. This difference is probably due to Stahler's estimation of the entire metabolic rate of each period of labor from the single determination of O_2 and CO_2 made during that period. From our records, it is believed that this is an inaccurate means of estimation, since wide and abrupt fluctuations occur in O_2 consumption in all phases of labor. Other obstetric details of these cases are recorded in Table III. Blood pressure and pulse rate observations were made at various times through labor, but no conclusion could be reached on their significance.

The practical significance of these estimates is that the total work done may be unimportant if accomplished over a longer period of time as illustrated in Case 39, Fig. 2, where there was a total excess intake of 60,560 c.c. of O_2 but an average of only 59 c.c. per minute, or about 20 per cent over basal rates. This represents no more than the lightest physical exercise.

On the contrary, the sudden load of work as accomplished between 4:30 P.M. and 6:10 P.M. in Case 42, Fig. 6, is represented by the approximate figure of 32,310 c.c. of excess oxygen consumed after 4:30

P.M. This is an average consumption of 150 per cent of the basal needs and represents between 8,092 and 16,155 Kg.-meters of physical work, or the work accomplished by a 50 Kg. individual climbing 161.4 to 322.8 meters, or from 40 to 80 flights of stairs.

Work is in progress at the University of California Hospital on blood volume, hematocrit, vital capacity, water balance, and circulation rate as well as blood pressure and pulse rate immediately prior to and succeeding delivery. A portion of this work has been reported in a preliminary publication¹⁶ and may give further clues to the mechanisms of circulatory strains and adjustments in labor.

Conclusions

1. A simple method is presented for the estimation of the degree and the time distribution of the work of obstetric labor by measurement of the oxygen consumption of the patient. Thirty-nine cases were studied.

2. In primiparous patients, the conclusion was drawn that a greater amount of work was done in a longer period of time than in multiparous patients as would be expected. Generally, in the first stage of labor, periods of increased oxygen consumption alternated with basal rates probably representing payment of oxygen debt, but the patient often demonstrated a slight excess oxygen intake one or more hours after delivery.

3. Multiparous patients rapidly increased their oxygen intake with delivery, but recovery of basal rates was prompt, often within half hour post partum.

4. Complicated deliveries were accompanied by a persistent elevation of oxygen consumption presumably caused by an increased circulatory load.

5. Five patients with rheumatic heart disease were studied. Two were free of symptoms and presented normal oxygen consumption curves; one had increased dyspnea and developed tachypnea, and a short period of very high rate of oxygen consumption during delivery; and one who was in heart failure at term, maintained a high oxygen intake post partum, and never regained her antepartum cardiac functional capacity. The fifth patient developed signs of serious failure during a prolonged first stage of labor and was uneventfully delivered by cesarean section with no consequential increase of oxygen intake.

6. The work of labor in both primiparous and multiparous women is the equivalent of mild to moderately heavy physical labor, the degree of which cannot always be predicted. In the presence of such a simple complication as a breech delivery, it may be increased markedly. This amount of physical work may be of the order that is commonly considered by clinicians as an unsafe risk for life or for maintenance of maximum function of cardiac patients in the ordinary routine of life. Cesarean section, whereas presenting other risks, does not carry the dangers of this unpredictable load of physical work, although postpartum cardiac death is reported to occur after this procedure for reasons as yet undetermined.

References

1. Boyer, N. H., and Nadas, A. S.: *Am. Int. Med.* 20: 99, 1944.
2. Hamilton, B. E., and Thomson, K. J.: *The Heart in Pregnancy and the Childbearing Age*, 1941, Boston, Little, Brown & Co., p. 96.

3. Hoffman, G. L., Jr., and Jeffers, W. A.: *Am. J. M. Sc.* 204: 157, 1942.
4. Hamilton, B. E., and Thomson, K. J.: *The Heart in Pregnancy and the Childbearing Age*, Boston, 1941, Little, Brown & Co., p. 101.
5. Cohen, M. E., and Thomson, K. J.: *J. A. M. A.* 112: 116, 1939.
6. Burwell, C. S.: *Am. J. M. Sc.* 195: 1, 1938.
7. Harrison, T. R.: *Failure of the Circulation*, Baltimore, 1935, Williams & Wilkins, p. 120.
8. Woodbury, R. A., Hamilton, W. F., and Torpin, R.: *Am. J. Physiol.* 121: 640, 1938.
9. Stahler, F.: *Abh. aus d. Geburtsch. u. Gynäk. u. Ihren Grenzgebieten* 7: 1936.
10. Lusk, G.: *J. A. M. A.* 70: 821, 1918.
11. Gagge, A. P.: *Science* 93: 551, 1941.
12. Shock, N.: *Personal Communication.*
13. Lusk, G.: *J. Biol. Chem.* 49: 41, 1924.
14. Margaria, R., Edwards, H. T., and Dill: *Am. J. Physiol.* 106: 713, 1933.
15. Hill and Flack, M.: *Am. J. Physiol.* 37: 27, 1909; 40: 347, 1910.
16. Sampson, J. J.: *West. J. Surg.* 51: 107, 1943.

THE COMPARATIVE ACTION OF POSTERIOR PITUITARY AND ERGONOVINE IN THE THIRD AND FOURTH STAGES OF LABOR*

Observations Based on 5,000 Deliveries

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THERE has been a considerable reduction in the maternal mortality in the last ten years, but deaths due to hemorrhage have not declined proportionately as have deaths from infection or toxemia. It behooves us to investigate further ways and means of controlling postpartum hemorrhage.

The oxytocics, posterior pituitary and ergot, are very potent in causing the uterus to contract, and they have been a great aid in the control of postpartum hemorrhage. In recent years ergonovine, which can be given intramuscularly and intravenously, and whose action is very prompt, has come into use. It is very effective in causing the immediate contraction of the uterus. We had great expectations that ergonovine would be the ideal drug to solve the problem of postpartum hemorrhage. Theoretically, it seemed logical that a drug which acts so promptly and produces firm contraction of the uterus should eliminate postpartum hemorrhage, but the results were not what we had hoped for.

We had used ergonovine intravenously or intramuscularly as soon as the placenta was expressed in over 2,500 deliveries. The uterus contracted firmly in less than one minute, but bleeding occurred, persisted, and recurred notwithstanding an apparently well-contracted uterus. For a time we were puzzled and at a loss to understand why that should be so, but now we believe we have an explanation for this occurrence.

In considering the physiology of the uterus during labor, we know that it involves a process of contraction and retraction of the uterine muscle fibers. There must be retraction together with contraction in order to produce dilatation of the cervix and to accomplish the expul-

*Read at a meeting of the Section of Obstetrics and Gynecology of the New York Academy of Medicine, Nov. 28, 1944.

sion of the fetus. The same process continues in the third and fourth stages of labor.

Ergot and its derivatives cause contraction of the uterus and maintain it in a tonic state of contraction but they do not produce retraction of the muscle fibers. To produce retraction, it is necessary to have rhythmic contractions and relaxations which recur intermittently. This is what takes place in normal labor and with posterior pituitary but not with ergot.

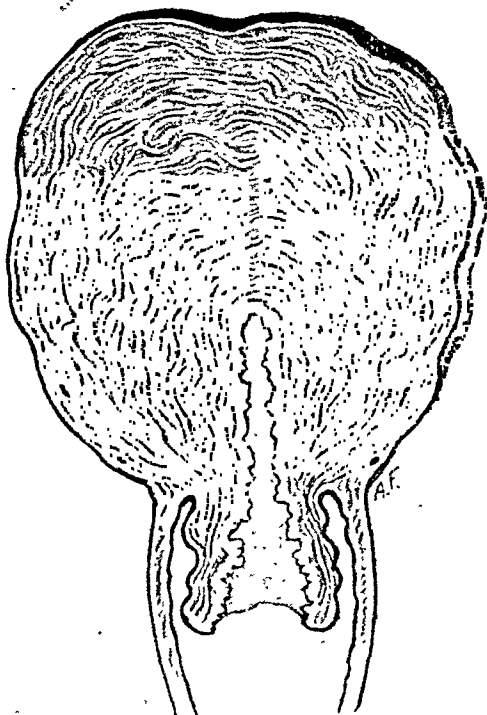


Fig. 1.

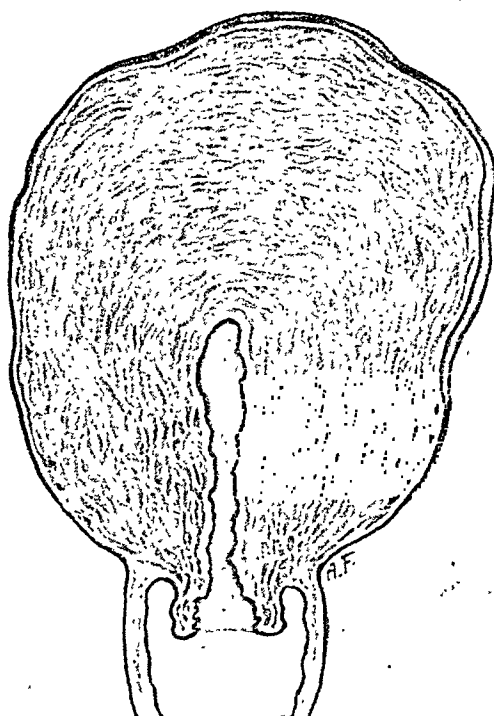


Fig. 2.

Fig. 1.—The uterus after ergonovine. The uterus is contracted, but the muscle fibers are not retracted. The cervix is elongated, relaxed, and flabby. The cervix hangs loosely in the vagina.

Fig. 2.—The uterus after posterior pituitary. The uterus is contracted, the muscle fibers are retracted, causing the bleeding sinuses to be obliterated. The cervix is retracted and is back to a normal state.

When ergonovine is given immediately after the placenta is delivered, the uterus goes into a state of tonic contraction, but retraction does not take place. The muscle fibers below the isthmus and the fibers of the cervix are not drawn up into the body of the uterus, but instead the cervix remains elongated, relaxed, and flabby, and hangs loosely in the vagina, while the body of the uterus and fundus are contracted (Fig. 1). We found this condition to be so by doing routine vaginal examinations in the third and fourth stages of labor. As the cervix and lower uterine segment are very vascular and congested during labor and as retraction does not take place, the bleeding vessels are not obliterated and as a consequence bleeding persists from this area notwithstanding a contracted uterus. In cases where there is a low insertion of the placenta, the bleeding from the congested area and sinuses may be considerable. When bleeding occurs with a firmly contracted uterus, it is, as a rule, attributed to a laceration of the cervix, but that is not necessarily so as the bleeding is more likely to be from a cervix that has not retracted.

When the uterus is contracted by the ergonovine and the cervix is not retracted but remains elongated and relaxed, the condition is un-

physiologic and it cannot remain that way for long. After a while the uterus must go through the process of retraction in order to take up the elongated fibers of the cervix. During this process the uterus will relax again and hemorrhage will recur. This is what causes hemorrhage to recommence after the uterus had been firmly contracted, and it explains the incidents where the patient starts bleeding again after having been put to bed in apparently good condition. Once bleeding sets in, the uterus fills up with blood clots and it is prevented from contracting properly. The vicious cycle can be controlled only by first removing the blood clots and then compressing the uterus bimanually.

We discontinued giving the ergonovine immediately after the placenta was expressed and now give posterior pituitary instead. When posterior pituitary is given intramuscularly immediately after the placenta is expressed, the uterus goes through the physiologic process of both contraction and retraction, and the fibers of the lower uterine segment and cervix are retracted into the body of the uterus. As a result, the bleeding areas are obliterated and the uterus and cervix return to a normal physiologic state (Fig. 2). During the period of contraction and retraction the uterus has to relax and contract several times and, as a consequence, some bleeding will, of necessity, occur, but this bleeding is unavoidable. However, when the process is over, the uterus and cervix are in the proper state. In order to reduce the bleeding to a minimum during this stage of contraction and relaxation, the uterus should be compressed bimanually, as outlined in a previous paper on the management of the third and fourth stages of labor (1939).

The posterior pituitary is given as soon as the placenta is expressed, which is in about two or three minutes after the baby is born. The action of the posterior pituitary lasts about twenty minutes, during which time the cervix is retracted; we therefore wait that length of time and give the ergonovine intramuscularly twenty minutes after the pituitary has been given but not before that time has elapsed. The ergonovine is purposely given intramuscularly, not intravenously, as we do not want it to act on the uterus too soon, that is, not before the full effect of the pituitary has been attained. In the interval, between the pituitary and ergonovine, repair of the perineum is done.

Ergonovine should not be given before pituitary extract nor at the same time with pituitary, for the reason that the ergonovine puts the uterus in a tonic state of contraction and the pituitary cannot exert its action of contraction and relaxation when the uterus is in a tonic state. The effect of the pituitary would thereby be nullified and it would not produce the necessary retraction.

When bleeding is severe, there is a temptation to give the ergonovine immediately or before the specified twenty minutes have elapsed. This should not be done as the results are not satisfactory. Instead, bimanual compression of the uterus should be practiced as previously indicated, and another ampule of pituitary may be given. Occasionally, posterior pituitary itself will put the uterus in a tonic state and it will have the same effect temporarily as the ergonovine. All we can do then is to wait until this abnormal effect wears off.

Neither posterior pituitary nor ergonovine should be given with the idea of hastening the separation of the placenta, as the placenta separates

by itself as soon as the baby is born and can be expressed in a few minutes, as I have already shown in a paper in 1929. This fact has recently (1942) been confirmed by Danforth, Graham, and Ivy in experimental work done on monkeys.

The management of the third and fourth stages of labor is therefore as follows:

When the baby is born, the cord is tied as soon as the baby has taken one or two deep breaths, but not before. The baby thereby expands its lungs and fills its system with as much blood as it can hold. We do not wait for pulsations in the cord to cease before tying it as the infant does not acquire more blood during the pulsations. If the pulsations were really an indication of blood circulating from the placenta, then the same quantity of blood would flow out of the baby as is supposed to flow into it.

A vaginal examination is made to ascertain whether the cervix has not contracted down on the already separated placenta and the placenta is promptly delivered as described in previous papers. One ampule (10 units) of pitocin is then given intramuscularly. Bimanual compression of the uterus is done to control and minimize the loss of blood in the interval that the pitocin is taking effect, and while the uterus is going through the process of contraction and relaxation.

When the bleeding is fairly well under control, a large wad of moist cotton is placed in the vagina and repair of the episiotomy or lacerations is commenced. The repair is not done before the placenta is delivered nor before the uterus is well contracted and bleeding is controlled.

During the repair, the nurse continues to hold the uterus firmly. If it relaxes or bleeding recurs, the sewing is interrupted and attention is immediately given to the uterus. The cotton sponge is removed from the vagina, vaginal examination is made, clots are removed, and the uterus is again compressed bimanually until the uterus is in a satisfactory state and the bleeding is under control. When the repair is completed, vaginal examination is again done, all clots are removed from the cervix and vagina, and the cervix is palpated to ascertain whether it has retracted.

We then wait the twenty minutes for the pitocin to have its full effect and only then give one ampule (0.2 mg.) of ergotrate intramuscularly. In this way we attain contraction of the uterus with retraction of the cervix and a firm tonic uterus.

If there is still some bleeding or oozing or if the uterus has a tendency to relax, we pack the vagina with iodoform gauze in order to fill up the vagina, so that when the uterus is held and compressed, it is pressed against a solid body rather than an empty space. I wish to repeat what I have maintained in previous papers, that packing the uterus is unphysiologic. Our object is to obliterate the bleeding sinuses, but by packing the uterus, the sinuses are instead distended and not permitted to contract. Bimanual compression of the uterus is a logical means of compressing the sinuses and controlling bleeding.

By giving the pituitary extract immediately after the placenta is delivered and postponing the ergonovine for twenty minutes, our results

have been very much more satisfactory in the last 2,500 cases than in the previous series.

Blood plasma and facilities for blood transfusions should be available, but we must not lose sight of the fact that prevention of the loss of blood is safer and more important than the most elaborate facilities for its replacement. Blood plasma cannot be considered a substitute for whole blood and should be used only while preparation is being made for the transfusion, but it should not delay the transfusion. Glucose and saline may do more harm than good if given while bleeding still continues, for the additional fluid, by raising the blood pressure, may aggravate the bleeding. Blood transfusions, when necessary, should be given as soon as possible; time should not be wasted by lulling ourselves into false security in depending upon substitutes. We must also realize that 500 c.c. of blood is not sufficient to replace four or five times that amount which may have been lost. When the veins are collapsed, it is being advocated that transfusion be given through sternal puncture. More attention must now be given to the Rh factor in transfusions; it is a real danger if ignored.

By managing the third and fourth stages of labor as outlined, we have had most gratifying results and transfusions were rarely necessary.

Summary

Posterior pituitary causes both contraction and retraction of the uterus and produces retraction of the cervix. It should be given immediately after the placenta is delivered.

Ergonovine causes a tonic contraction of the uterus but no retraction and should only be given twenty minutes subsequent to the posterior pituitary extract when retraction of the cervix has already taken place.

The management of the third and fourth stages of labor is reviewed.

References

- Danforth, D. N., Graham, R. J., and Ivy, A. C.: *Surg., Gynec. & Obst.* 74: 188, 1942.
DeLee, J. B., and Greenhill, J. P.: *Principles and Practice of Obstetrics*, ed. 8, Philadelphia, 1943, W. B. Saunders Co.
Ivy, A. C.: *AM. J. OBST. & GYNEC.* 44: 952, 1942.
Ivy, A. C., and Rudolph, L.: *Surg., Gynec. & Obst.* 67: 188, 1938.
Leff, M.: *AM. J. OBST. & GYNEC.* 18: 868, 1929.
Leff, M.: *Surg., Gynec. & Obst.* 68: 224, 1939.
Reynolds, S. R. M.: *Physiology of the Uterus*, New York, 1939, Paul B. Hoeber, Inc.
Titus, Paul: *Management of Obstetric Difficulties*, ed. 2, St. Louis, 1940, The C. V. Mosby Co.

SUPRAVESICAL EXTRAPERITONEAL CESAREAN SECTION (WATERS' TYPE)*

Experience With 250 Operations

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(From the Margaret Hague Maternity Hospital)

RESULTS achieved determine the worth of any operation. Factors conditioning these results vary with the era and the operator, so that one recurrently experiences changes influencing surgical practice. Thus, hazardous and awe-inspiring procedures of one generation become routine performances in the next. Critical comment on any operation is predicated, therefore, upon judicious consideration of its need, advantages, dangers, complications, and results, during the period in which it is offered.

Our purpose is to review experiences with one operation, the supravescical extraperitoneal cesarean section as proposed by the author, and to resubmit various anatomic and operative data concerning it.

It is proper that this operation, by no means new, has gained its rightful place in the operating obstetrician's armamentarium because of factors and considerations either not available or not applied in its older experience.

Without presuming to review its history, which has been dealt with adequately and often, we would like to recall again one anatomic fact closely related to the historical development of extraperitoneal cesarean section. This fact, overlooked throughout the years, is that there are but *two anatomically possible ways to reach the uterus extraperitoneally*, due to the situation of the pregnant uterus in the pelvis, and the location of the peritoneal reflections from its lower segment onto other organs or the pelvic side walls. One possibility is to reach the lower anterior extraperitoneal uterine segment from an approach lateral to the bladder, through the paravesical space. It was recognized and tried in 1821 by Ritgen. Fundamentally, the operations of Baudelocque, Thomas, Skene, and Latzko, in spite of variations in abdominal wall incision and approach, fall into the same group. Of these operations, the Latzko technique is the most popular.

The only other possible way to reach the lower uterine segment extraperitoneally is by a supravescical approach. Physick of Philadelphia in 1824 first proposed this approach to DeWees in Horner's letter. It was not attempted until 1908-1909 when Frank and later Sellheim unsuccessfully tried it. This same approach is the basis for the series of operations I presented in January, 1939. It possesses one radical difference; the plane of dissection. Whereas previous operators attempted to "peel" the peritoneum from the bladder and pelvic fascia, an almost impossible undertaking, the peritoneofascial flap was here "lifted" and dissected as a unit, a perfectly feasible and not too difficult surgical procedure. Therein lies the difference between success or failure in a

*Presented before the Philadelphia Obstetrical Society, Feb. 3, 1944.

rather old procedure, and it is the only modern major contribution to the technique.

To comprehend adequately the surgical technique, an understanding of the investments of the uterus and the bladder is invaluable.

The peritoneum covers the pelvic organs, adapting itself to the bladder, uterus, and bowel in their varied stages of distention. From the anterior abdominal wall, the peritoneum reaches the bladder to cover its superior surface and descend for a short distance over its posterior surface, whence it is reflected upward on the anterior surface of the uterus, thus forming the uterovesical pouch. Laterally from the bladder, the peritoneum bridges the lateral vesical (paravesical) spaces to reach the pelvic side walls, while the lateral reflections from the uterine surfaces to the pelvic walls form, respectively, the anterior and posterior surfaces of the broad ligaments.

In passing from the abdominal wall to the bladder, the peritoneum is lifted by fibrotic cordlike remnants of fetal structures. The obliterated urachus forms the middle umbilical ligament, extending from the apex of the bladder to the umbilicus. The lateral umbilical ligaments, the fibrotic reminders of the once important umbilical or hypogastric arteries, extend from the umbilicus to the bladder lateral to its apex, and vary considerably in size in different women. They are frequently insignificant. The proximal portions of these structures between the bladder and the internal hypogastric arteries persist as vesical arteries. The "draping" of the peritoneum over these ligaments forms depressions, those between the middle and lateral ligaments comprising the supravescical fossae, and those outside of the lateral umbilical ligaments forming the paravesical fossae.

Loose subperitoneal tissue lies between the peritoneum and the pelvic fascia. In certain areas, notably lateral to and behind the bladder and in the base of the broad ligaments, this areolar tissue is well packed with soft fat, filling the spaces between the peritoneum and fascia. Over such areas the peritoneum is loosely applied, whereas over the bladder fundus it is less developed. On the anterior uterine surface, the interposed subperitoneal areolar tissue is extremely thin. The vessels and nerves of the pelvis lie within its substance, and perforate the fascia to reach the viscera. The vesical vessels perforate the fascia vesicae (*quod vide*) inferolaterally to lie between the fascia and the bladder muscularis. This is a fact of considerable clinical importance. In considering the pelvic fascia, I like to regard it as fulfilling two purposes, i.e., support and envelopment, with the basic and more important function being support. The supporting portion of the endopelvic fascia represents a continuation into the pelvis of the transversalis fascia of the abdomen. It is reflected medially just above the origin of the levator ani muscle and forms with it the upper pelvic diaphragm. Within its substance, and developed in response to functional needs, are condensations of fibers which constitute the well-known pubovesical, cardinal, uterosacral, etc., ligaments. These form, with the broad spread of the endopelvic fascia, the supporting portion.

The investing fasciae develop from the upper pelvic diaphragmatic fascia at the sites of visceral penetration. The bladder is surrounded by it, and thus we have the fascia vesicae or perivesical fascia. Fascia

extends upward to cover the uterus as the fascia uteri or periuterine fascia, and the downward prolongation becomes the vaginal fascia. The investing fasciae of bladder and uterus are adjacent and intimately fused at their origins from the supporting layer of endopelvic fascia, where the bladder base and cervix are held together by the tough pubovesicocervical ligaments.

In the latter part of pregnancy, changes take place in visceral relationships and in the pelvic tissues. The bladder is flattened anteroposteriorly and when distended reaches higher in the abdomen. This, with the growth of the uterus, elevates and loosens the vesico-uterine pouch of peritoneum. The thickened elongated round ligaments lift the peritoneum from the lateral walls of the false pelvis. The pelvic tissues, notably the subperitoneal connective tissue, share in the physiologic increase of intracellular and extracellular water. The distention of the lower uterine segment thins the cervical and uterine fascia and pubocervical ligaments, and separation from the viscera becomes relatively easy. The laminated character of the fibro-elastic fascial envelopment of the bladder is evident at every operation.

From the foregoing, it is clear that one may reach the uterus without entering the peritoneal cavity, by passing between the bladder fascia and its muscularis. An abdominal incision opens the space of Retzius, then an incision in the bladder fascia opens the external end of a tunnel-like approach to the uterus. This artificially created "abdominal-vagina" is developed by further lifting the fascia vesicae with the overlying peritoneum. At the inner end, the fascia vesicae and fascia uteri must be incised to permit elevation of the uterovesical pouch of peritoneum, to complete the extraperitoneal subfascial tunnel from abdominal wall to uterine muscle. Thus the roof of this tunnel is the elevated peritoneum which covered the bladder and vesico-uterine space, with the attached fascia resected from the dome of the bladder and the lower uterine segment. The base of the tunnel is the denuded bladder and the pubocervical fascia. The lateral tissue is the fascia spread from the lateral umbilical ligaments, which marks the extent of the supravescical fossa.

The foregoing clarifies the description of the operation and includes the latterly developed features.

Operative Preparation

Prophylaxis.—The patient is typed, and cross-matched bank blood of the same type is assured. All bleeding cases and any with pre-existing anemia are typed, cross matched, and suitable blood readied before operation. Dehydration is treated if present, and lavage done on vomiting patients.

Vaginal.—The vaginal orifice and tract are thoroughly antiseptized and a careful and complete vaginal examination made. The fetal head, if fixed, is pushed well upwards to facilitate its later extraction as recommended by Jellinghaus. An indwelling catheter is inserted into the bladder, and tested for free inflow and outflow. It is connected to an irrigator containing a sterile solution of water colored with methylene blue. Prior to abdominal incision, the bladder is filled with 150 to 200 c.c. of solution, or enough to obtain moderate distention. This is maintained until bladder dissection is well advanced.

Abdominal.—The abdomen is thoroughly cleansed and prepared for incision with an efficient antiseptic. It is draped to expose a low operative field between umbilicus and symphysis.

Instruments.—Fritsch abdominal retractors are best for retracting the bladder below and the peritoneofascial flap above. For lateral retraction, Richardson 1½ inch retractors are least traumatic. Adequate exposure through good retraction is essential.

After the initial central "nick" in the uterine wall, bandage scissors are used to complete the crescentic incision. One blade of an Elliott or Simpson forceps is used as a vectis to deliver the baby's head. Constant suction is employed after the uterus has been opened, to clear the operating field.

The incised uterine wall is best held with De Lee T-clamps.

The Operation

The abdominal incision is a left lower rectus "trap door" from pubes to two-thirds of the umbilicus. The pyramidalis is separated from the lower end of the rectus muscle. Or Pfannenstiel's incision, which is satisfactory, may be chosen.

After retracting the rectus muscle laterally, the already distended bladder may be seen through the overlying transversalis and perivesical fasciae. The relatively thin transversalis fascia with some thickened transverse trabeculae is incised vertically. A "T" shaped incision is made in the perivesical fascia in the following manner: A 1-inch vertical incision is made through the laminated fascia covering the distended bladder down to its muscularis, at a point about two-thirds of the distance up on the exposed bladder. The Bard-Parker knife handle is inserted downward between bladder fascia and muscularis, the tissue freed, and the fascia then divided vertically with a Mayo scissors. This permits the filled bladder to herniate forward. (The vesical vessels lie between fascia and muscularis, and serve to orient the operator.) The cross of the T incision in the fascia, which must be generous, is made by insinuating curved Mayo scissors between bladder fascia and muscle and dissecting as in a cystocele operation, cutting after visualizing. The fascia, though laminated, is easily separable as a unit with knife handle and Mayo scissors. Laterally it fans out and thins where it contains enmeshed fat tissue. At the urachus it is adherent, and when a large exposure is needed, the urachus must be "surrounded" by dissection, doubly tied and cut, lest the peritoneum be torn there.

The peritoneofascial (P.F.) flap or fold is now lifted upward by Mayo scissors and knife handle dissection keeping close to the bladder muscle. The dissection proceeds over the top and left upper corner of the bladder, seeking the most accessible portion of the uterovesical fold of peritoneum.

It is best to empty the bladder at this stage. The P.F. flap and bladder are now drawn apart using gauze, until the uterovesical plica is identified lying against the lower segment. (The lower segment is now being viewed through the posterior portion of the fascial envelope of the bladder and the uterine fascia over the lower segment.)

An incision is made below the hernial saclike fold of uterovesical peritoneum and through the fascial layers noted, down to the glistening muscularis of the lower segment. The finger is inserted then beneath these fasciae, and the fascia and bladder are stripped and freed from the front of the lower uterine segment. (This is comparable to the procedure, in lower segment transperitoneal cesareans, whereby the bladder is freed from the lower uterine segment.)

Obviously, to expose a large lower extraperitoneal segment it is now necessary to cut through the posterior portion of the perivesical fascia still attached to the bladder, starting with the initial opening below the hernia-like plica. This is done by knife dissection, using the handle to push the bladder muscularis away. This permits visualization of the intact P.F. fold before cutting the fascia close to the bladder, where-

upon the P.F. fold is completely freed of attachment and lifted upward from the bladder. The bladder is dropped below the pubis and retracted with a Fritsch retractor. Lateral fascial retraction is obtained with 1½ inch Richardson retractors.

A centrally placed transverse "nick" is made in the exposed uterine segment 1½ inches above the depth of the bladder effacement, down to membranes. Cultures are taken from amniotic sac (and later, after removing the fetus, from the cervical segment). With a bandage scissors placed in the "nick," a crescentic incision is carried in either direction, first to left, then right, the ends reaching a level about 1½ inches above the "nick." The size of the baby's head determines to a degree the acuteness of the curve. The ends always avoid the broad ligaments. No attempt is made to control any uterine wall bleeding until the baby has been removed from the uterus.

In vertex presentations, one blade of a forceps is passed in laterally, then swung below the disengaged head and used as a vectis to pry and lift out the head, with strong fundal counterpressure being exerted to facilitate delivery. It is best first to turn the head so that the occiput presents in the wound and birth is by extension. Breech deliveries are simple, and internal versions may be performed. The baby is removed, and the edges of the wound grasped with T-clamps using one at each end and one in the center of each crescent. Ergotrate is given intravenously and the placenta and membranes are immediately extracted manually.

Two layers of No. 1 chromic single sutures are placed in the uterus. The first is a running stitch beginning at the left end of the incision with stitches placed accurately and closely. The second layer is a Cushing continuous stitch, completely inverting the first. In the event of uterine wound infection, discharge into the cervical segment and lochia is effected. This suture also produces direct uterine fascial approximation, a most important factor in sound uterine wall healing.

The operative area is dried and No. 0000 chromic ties placed on any bleeding points. "Sulfa" powder is sprinkled (not packed) over the retrovesical tissues and a Penrose rubber tissue drain placed in the retrovesical space and brought out of the lower end of the wound. The peritoneofascial flap is replaced over the bladder from whence it was lifted by dissection. Fine interrupted sutures reapproximate the left rectus to the median raphe. The rectus fascia is sutured with continuous No. 1 chromic catgut and the abdominal wall closed with silk or Michel clips.

Certain minor variations in technique may be employed, depending upon the patient and the operator. For identification, the amount of bladder fill may vary from none to 400 or 500 cubic centimeters. Fascial identification and the "T" incision in the fascia are simpler with a well-filled bladder, but further fascial dissection is easier and quicker with the bladder nearly empty. An overdistended bladder or one with a large fundal "air-bubble" is easily perforated. The inserted catheter alone may serve as a guide to bladder outline.

To briefly review the manner of fascial incisions, it is seen that first the thin transversalis fascia is incised. Then the perivesical fascia is divided as it covers the fundal portion of the bladder near the parietovesical peritoneal reflection. After separation of this, especially over the left upper bladder angle, the same layer is again incised posteriorly to expose the fascia covering the lower uterine segment. Thus the bladder is "denuded of a fascial-skullcap" which remains attached to the peritoneum, from bladder fundus to the uterovesical pouch. This permits the peritoneum to be freely and easily lifted and the bladder dropped below the symphysis behind a Fritsch retractor. Transverse incision of uterine fascia over the lower segment increases the mobility of the uterine peritoneum. The rest of the operation is essentially a laparotrachelotomy with (Kerr) transverse crescentic incision through the lower uterine

segment. The exposed field permits any type of uterine wall incision but the transverse crescent is by all odds the best.

Postoperative Care.—The drain is left in two to five days, depending upon the infectivity of the case. The catheter is left in two days to rest the bladder. Prostigmine (P) is given every 4 hours for 24 hours; then every 6 hours for 24 hours, with rectal tube for $\frac{1}{2}$ to 1 hour after each injection. Patients are usually permitted fluids immediately, soft diet in twenty-four hours and regular diet in forty-eight hours. Intravenous fluids and blood transfusions are used on the slightest indication.

Statistical Data and Comment

The tables setting forth the statistical data are self-explanatory. There are certain inclosures which bear emphasis and comment. These are offered for the benefit of the fortunately diminishing groups offering classical sections as routine operations for all but the "lost hope" patients.

The total cesarean incidence is 2.67 per cent. Of 1,837 cesareans in this twelve-year period, 23.4 per cent were of some extraperitoneal type. This incidence reflects the demonstrated safety and progressive use of the operation. In the past six years, most of these have been of the type described by the author. Our experience in the 431 extraperitoneal sections, including 250 of the supravescical type, demonstrates such a low mortality that we almost never use a Porro operation, do a craniotomy on a living child, or hesitate to use it where we believe an intrauterine infection is probable or even remotely possible. The figures in Table II are absolute. The vast majority of the extraperitoneal operations were performed on bad risk patients. In Table III are tabulated the cases with established sepsis before or during labor. Yet of the maternal deaths in the supravescical group, only one died from sepsis although the major cause of death from all cesareans listed was sepsis in some form.

Who can study the comparative data in this table of nearly 2,000 cesarean sections of various types and say that extraperitoneal sections are hazardous, rarely indicated, suggest bad handling of material, are too difficult, or incorporate a high mortality rate? The rather moderate technical difficulty of the extraperitoneal operation is certainly no excuse for failing to perform it where the indication is present, and the indication should be *any potentially infected case*. To reserve it solely for badly infected or septicemic patients is comparable to awaiting appendiceal rupture and peritonitis before operating. If the reader will scrutinize the mortality table, he will understand why we unequivocally insist upon a low cervical-segment operation for elective and clean cases and extraperitoneal operation for any in which a "reasonable doubt" exists.

Employing the technique described in this paper, there were four bladder perforations in the 250 extraperitoneal sections. There were no persisting fistulas, since all perforations are easy to see and repair. Unless there is a pyelocystitis, puncture of the bladder, though certainly not recommended, is totally unimportant. But peritoneal punctures may be very dangerous. Although the number is high, it is lower, we believe, than previously reported for any considerable number of extraperitoneal sections. All but two, however, were made, recognized, and repaired *before* the uterus was incised. In other words, *in only two cases was*

TABLE I. GENERAL CESAREAN SECTION DATA—OCTOBER, 1931, TO JAN. 1, 1944

	NUMBER	PER CENT	INCIDENCE
Total deliveries	68,786	0.278	or 1 in 360
Maternal mortality	191	2.67	or 1 in 37.4
Total cesareans	1,837	1.52	or 1 in 66
Cesarean mortality	28		

TABLE II. TYPE OF CESAREAN OPERATIONS

	NO.	MORTALITY NO.	PER CENT
Transperitoneal and exclusion types	1261	13	1.03
Extraperitoneal cesareans	431	5	1.16
a) Waters' supravescical	250	2	0.8
b) Latzko's paravesical	181	3	1.65
Classical	117	8	6.8
Hysterectomy (Porro)	27	2	7.4
Vaginal	1		
Postmortem (cesarean section)	10		

TABLE III. SUPRAVESICAL EXTRAPERITONEAL CESAREAN (WATERS)

Total cases, 1937 to Jan. 1, 1944	250
Deaths	2 or 0.8%
Preoperative morbidity and sepsis	90 cases
Uterine cultures at operation—60 positive, 56 with pathogenic bacteria, 2 septicemia	
<i>Anesthesia</i>	
Spinal	190
Spinal plus ether	51
Operating time—Average, first 75 cases	36 min.
Commonly	40-60 min.
Number of operators	29
<i>Complications:</i>	
Bladder perforations	4
Persisting fistulae	0
Pulmonary embolism	1
Peritoneal punctures	68 or 27% (All but two occurred <i>before</i> opening uterus; 23 in "first" operations 4 deliberate for postoperative tubal ligation)

there peritoneal cavity communication with an infected operating field. The safety factor thus achieved in this operation is an asset of utmost importance.

The type of anesthesia reduces mortality. For more than fifteen years we have used spinal anesthesia for cesarean section. Two hundred and forty-one of the 250 extraperitoneal cases here reported were given either spinal anesthesia alone (190) or spinal with some terminal anesthesia. We believe it to be one of the safest anesthetics for cesarean section, all things considered. No spinal death is ever explained away, wherever it happens. Irrespective of attendant factors and conditions which might have made *any* anesthetic a great risk, the agent employed bears the full responsibility. With any agent other than spinal, a death under anesthesia is commonly attributed to attendant conditions necessitating or influencing the operation. This attitude is obviously unfair and prejudices honest appraisal of the anesthetics used. In this instance, a consideration of the total deaths from *all* causes in 250 operations, where 241 had spinal anesthesia, is advised. If this form of anesthesia produced the bad results promised by those who neither use it nor possess substantiating experience, we would not recommend it after fifteen years of use on thousands of parturient women.

In conclusion, it is felt that the experiences provided by these 250 supravescical extraperitoneal cesareans prove it to be a safe and satisfactory routine operation for any potentially infected patient requiring cesarean section.

References

- Ritgen, F. A.: *Heidelberger Klin. Annal.* 1: 263, 1825, pt. 2.
 Baudelocque: *Rev. méd. franç. et étrangère*, 1824.
 Thomas, T. G.: *Am. J. Obst. & Dis. Women* 3: 125, 1870; 8: 326, 1875.
 Chambers, P. F.: *Am. J. Obst. & Dis. Women* 47: 502, 1903.
 Latzko: *Zentralbl. f. Gynäk.* 20: 131, 1908; 33: 769, 1909; *Wien. klin. Wchnschr.* 22: 477, 1909.
 Norton, J. F.: *AM. J. OBST. & GYNEC.* 30: 209, 1935.
 Burns, H. T.: *AM. J. OBST. & GYNEC.* 19: 759, 1930; 28: 556, 1934.
 De Wees, W. P.: (Physick reference) *Compendious System of Midwifery*, ed. 8, 1839, p. 598.
 Frank, F.: *Arch. f. Gynäk.* 81: 46, 1906; *Zentralbl. f. Gynäk.* 5: 593, 1881.
 Sellheim, H.: *Zentralbl. f. Gynäk.* 133, 319, 641, 1297, 1908; *Medical Ann.* 226, 1911 (Trans. by E. W. Hey Groves); *Monatschr. f. Geburtsh. u. Gynäk.* 34: 34, 1911.
 Waters, E. G.: *AM. J. OBST. & GYNEC.* 39: 423, 1940.
 Kehrer, F. A.: *Arch. f. Gynäk.* 19-20: 177, 1882; *Beitr. z. Geburtsh. u. Gynäk.* 17: 206, 1912.
 Kerr, J. M. M.: *J. Obst. & Gynec. Brit. Emp.* 28: 475, 1921; *Proc. Roy. Soc. Med.* 29: 1645, 1936.
 Krönig, B.: *Operative Gynäkologie*, ed. 3, Leipzig, 1912, p. 879.
 Küstner, O.: *Der abdominale Kaiserschnitt* (Deuts. Frauenheilk., ii), 1915.
 Furniss, H. D.: *AM. J. OBST. & GYNEC.* 19: 849, 1930.
 Waters, E. G.: *AM. J. OBST. & GYNEC.* 29: 535, 1935.

39 GIFFORD AVENUE

SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION IN WOMEN*

(Sulfanilamide, Sulfapyridine, Sulfathiazole, and Sulfadiazine)

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THE value of sulfonamide therapy in gonococcal infection has been well established and we have not attempted to review the literature. Generally, conclusions concerning the effectiveness of the various drugs have been based primarily upon results obtained in men. The part women can play in the spread of this infection, however, makes it imperative that their treatment be evaluated accurately. It is essential to determine: (1) to which sulfonamides these women respond most surely and promptly; (2) how long organisms may be harbored with few or no symptoms; (3) when the carrier state ends; and (4) whether so-called "drug-fast" strains are produced frequently.

This report is the result of a four-year study of sulfonamide therapy in gonococcal infection in women.† A sufficiently large series of women

*This work was done under a grant from the Albert B. Kuppenheimer Foundation, the Department of Obstetrics and Gynecology, the University of Chicago and the Chicago Lying-in Hospital.

†Most of the patients in this study were made available through Dr. Herman N. Bundesen, President of the Chicago Board of Health, and Dr. G. G. Taylor, Director of Syphilis and Gonorrhea Section of the Municipal Social Hygiene Clinic of Chicago.

were treated with each of the sulfonamides* to draw accurate conclusions concerning the best methods of diagnosis and treatment, and to determine the drug of choice and the necessary criteria of cure of the infection.

During the course of this investigation, 1,126 women were treated with sulfanilamide, sulfapyridine, sulfathiazole or sulfadiazine. Our criteria of cure required that the patients be observed at least two months following therapy before they could be discharged as cured. Consequently, 551 patients who responded to treatment but became delinquent before the observation period was completed have been deleted. The remaining 575 patients who were discharged as cured, or who failed to respond to therapy are considered in detail here. Of these, 430 (75 per cent) responded to one course of therapy and were discharged cured; 145 had repeated or recurrent positive cultures and received further therapy.

Probably the most difficult problem in the evaluation of treatment of an infection such as gonorrhea lies in the differentiation between reinfection and actual failure of the patient to respond to treatment. Considerable time and effort were expended upon those patients who had recurrent positive cultures, and every possible means was utilized to determine the cause. Much of the credit for the final differentiation is due to residents and interns who cooperated in this study and succeeded in eliciting the confidence of the patients as well as their cooperation.

If the patient admitted sexual intercourse, or if smears showed the presence of spermatozoa, reinfection was considered to have taken place. Our efforts to find and determine the infectiousness of the partner were not too successful, and we realize that the recurrence of positive findings may have been due to exacerbation of a latent infection rather than reinfection. For that reason, failure of therapy has been computed in two ways. One method excludes the patients from whom evidence of intercourse and possible exposure to infection were obtained; the other method includes them as possible failures. We believe that most of these patients actually became reinfected, but in a series less well controlled and checked, they might have appeared as "drug failures." On several occasions, patients had been studied several weeks or even months and had received repeated courses of therapy before we discovered that they were being constantly exposed to reinfection.

Methods

All of the patients were ambulatory. A few of them were treated at the Max Epstein Clinic of the University of Chicago, but most of them were from the Chicago Municipal Social Hygiene Clinic. Fifty-one patients were pregnant. Eighty-five per cent were Negroes.

Diagnosis and Criteria of Cure.—The plan of procedure in the study of patients was outlined in detail in previous papers.¹⁻³ Diagnosis in

*The sulfonamides used in this study were furnished through the courtesy of the Medical Research Departments of: (1) Winthrop Chemical Company, New York City, (sulfanilamide and sulfathiazole); (2) Merck and Company, Rahway, N. J., (Sulfapyridine); and (3) Lederle Laboratories, Incorporated, Pearl River, N. Y. (sulfadiazine).

every case was based on isolation and identification of the gonococcus in pure culture. Cure was determined by routine cultures and smears taken two or three times a week during treatment, twice a week for the first month after cultures had become negative, and at least once a week thereafter. Smears and cultures were also taken during and just following the menstrual period. The provocative test, which consisted of application of 10 per cent silver nitrate to the cervix and 5 per cent silver nitrate to the urethra was performed on the first or second postmenstrual day. Cultures were taken just before silver nitrate was introduced, and on the first and fourth days subsequently.

At first our criteria of cure required that patients have negative cultures and smears through three menstrual periods and two postmenstrual provocative tests. Practically, this proved to be too rigorous a requirement although 235 patients did fulfill it. Of these, only two patients in whom there was no evidence of reinfection had recurrent positive cultures during the third month of observation, but both of them became delinquent before failure of therapy could be substantiated.

All of the 575 patients considered here have been observed through two negative menstrual periods and one postmenstrual provocative test. Patients who did not menstruate (12 were postmenopausal and 18 had had hysterectomies) were observed for two months and received two provocative tests. The 51 pregnant patients were not given provocative tests, but were checked by smears and cultures taken about six weeks post partum.

Treatment.—Sulfanilamide, sulfapyridine, sulfathiazole, and sulfadiazine were used in the treatment of this infection. Patients were assigned in rotation to the various drugs insofar as it was practical. Four doses of drug were given daily and six days constituted a course of treatment with all drugs except sulfanilamide, which was given for fourteen days. The dosage schedules for each of the drugs are listed in Table I.

TABLE I. SULFONAMIDE DOSAGE IN AMBULATORY CASES OF GONOCOCCAL INFECTION IN WOMEN

DRUG	DAILY DOSAGE*		NO. OF DAYS	TOTAL NO. OF DAYS	TOTAL DOSAGE	
	GRAMS	GRAINS			GRAMS	GRAINS
Sulfanilamide	4	60	4	14	42	630
	2.6	40	10			
Sulfapyridine or	3	45	2	6	14	210
Sulfathiazole	2	30	4			
Sulfadiazine	2	30	6	6	12	180

*Divided into four doses as nearly equal as practical in amounts and at about five-hour intervals, or from first to last dose a time lapse of 15 hours.

If a patient failed to respond to one course of treatment or became reinfected during the period of observation, a second course of the same drug was occasionally tried, but usually a different sulfonamide was used. Three to seven days usually intervened between courses of treatment.

Only one course of treatment was required to effect a cure in 430 (75 per cent) patients; 4 who were still infectious after one course of therapy became delinquent. More than one course of treatment was given 41 patients who failed to respond to the initial therapy and to 101 patients who were presumably reinfected. Forty-five patients received two or three courses of the same drug. Of those given only one drug, 98 received sulfanilamide, 128 sulfapyridine, 151 sulfathiazole and 102 sulfadiazine. Ninety patients received two drugs and six received three drugs. The number of courses of therapy, with the same or different drug, required in treatment is listed in Table II. In Table III, are

TABLE II. NUMBER OF PATIENTS AND COURSES OF TREATMENT RECEIVED

NO. PATIENTS		NO. COURSES	
430	1 course—discharged cured	430	
4	1 course—became delinquent—infectious	4	
141	More than 1 course	324	
	96 2 courses	172	
	32 3 courses	96	
	10 4 courses	40	
	2 5 courses	10	
	1 6 courses	6	
Total 575		758	

TABLE III. NUMBER OF PATIENTS TREATED WITH EACH DRUG AND THE NUMBER OF DRUGS RECEIVED BY EACH PATIENT

DRUG	ONE COURSE ONE DRUG	MORE THAN ONE COURSE			TOTAL PATIENTS TREATED WITH EACH DRUG
		ONE DRUG	TWO DRUGS*	THREE DRUGS†	
Sulfanilamide	89	9	38	5	141
Sulfapyridine	114	14	46	6	180
Sulfathiazole	134	17	72	6	229
Sulfadiazine	97	5	24	1	127
Total Therapies	434	45	180	18	677
Total Individuals	434	45	90	6	575

*17 patients received sulfanilamide and sulfapyridine

21 patients received sulfanilamide and sulfathiazole

28 patients received sulfapyridine and sulfathiazole

1 patient received sulfapyridine and sulfadiazine

23 patients received sulfathiazole and sulfadiazine

†5 patients received sulfanilamide, sulfapyridine and sulfathiazole

1 patient received sulfapyridine, sulfathiazole and sulfadiazine

shown the number of patients who received each drug and the number of drugs given each patient. Since one patient might receive two or three drugs, the total number of different patients receiving the various drugs was 677 although only 575 individuals were studied. A total of 141 patients were given sulfanilamide, 180 sulfapyridine, 229 sulfathiazole and 127 sulfadiazine.

Results

The responses to the various drugs shown in Table IV have been listed under the headings "cure," "reinfection" and "failure." Those patients considered cured were observed through two negative menstrual periods and one postmenstrual provocative test before they were discharged. Of the patients treated with sulfanilamide, 71 per cent were discharged cured, with sulfapyridine 82 per cent, with sulfathiazole 87 per cent and with sulfadiazine 94 per cent. Six patients required two

TABLE IV. RESPONSE TO SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION IN WOMEN

	SULFANILAMIDE			SULFAPYRIDINE			SULFATHIAZOLE			SULFADIAZINE		
	CURE	REINFECTED	FAILURE	CURE	REINFECTED	FAILURE	CURE	REINFECTED	FAILURE	CURE	REINFECTED	FAILURE
One course	86			113			134			97		
Repeated courses— 1 drug	0		22	2		9	3		6	1		1
Reinfection	9	18*		12	21*		14	20*		4	5*	
Repeated courses— 2 to 3 drugs	0		1	9		3	19		2	4		1
Reinfection	5			11			31			14		
Subtotals	100	18	23	147	21	12	201	20	8	120	5	2
Total		141			180			229			127	

*Discharged or delinquent subsequent therapy.

or more courses of the same drug to effect cure, but since they were eventually cured by one type of therapy, the initial failure to respond to treatment was not listed with the "drug-failures."

The patients listed in the "reinfection" group responded to therapy, but had recurrent positive cultures during the period of observation. All of them either admitted sexual intercourse, or spermatozoa were found on the smears. Presumably most of these patients were cured and then were reinfected, but they did not fulfill the criteria of cure. (Some of them may have had an exacerbation of a latent infection brought about by intercourse.) Facilities were not available for us to ascertain the state of infectivity of the partner except in a few instances. In those cases, cure was effected after both partners had been treated. In Table V, the reinfections (sulfanilamide 13 per cent, sulfapyridine 12 per cent, sulfathiazole 9 per cent and sulfadiazine 4 per cent) have been listed separately and also grouped with the failures. The latter figure is undoubtedly higher than the actual percentage of patients that failed to respond to therapy, but probably corresponds to the figures obtained in studies where it was impossible to investigate the problem of reinfection.

TABLE V. EFFICACY OF SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION IN WOMEN

	TOTAL	REINFECTION		TOTAL FAILURES		NUMBER OF PATIENTS DISCHARGED CURED	
		NO.	%	NO.	%	NO.	%
Sulfanilamide	141	18	13	23	16	100	71
Sulfapyridine	180	21	12	12	6	147	82
Sulfathiazole	229	20	9	8	4	201	87
Sulfadiazine	127	5	4	2	2	120	94

TABLE VI. FAILURE OF SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION IN WOMEN—REINFECTIONS DELETED

	NO. OF PATIENTS	TOTAL FAILURES		SECONDARY FAILURE*		INITIAL FAILURE†	
		NO.	%	NO.	%	NO.	%
Sulfanilamide	123	23	19	1	2	22	17
Sulfapyridine	159	12	8	3	2	9	6
Sulfathiazole	209	8	4	2	1	6	3
Sulfadiazine	122	2	2	1	1	1	1

*Failure following failure on one or more sulfonamides previously.

†Failure on first drug received.

Patients who failed to respond to therapy and in whom there was no evidence of exposure to reinfection were considered failures. With sulfanilamide, there were 23 patients (16 per cent), with sulfapyridine 12 (6 per cent), with sulfathiazole 8 (4 per cent) and with sulfadiazine 2 (2 per cent). Since some of these failures were in patients who had failed to respond to previous sulfonamide therapy, it may have been that drug-fast strains were produced by the initial therapy. The true failures are probably those listed in Table VI, from which the group of patients who had been exposed to reinfection has been deleted, and in which initial and secondary failures have been separated.

In Table VII, are shown the results of subsequent therapy in those patients, who failed to respond to the first drug used.

Pregnant Patients.—Nine of the group of 61 pregnant patients (15 per cent) failed to respond to initial therapy, whereas the failure rate in the whole group of 575 patients was only 7 per cent. Four of the patients aborted, and in two of them, cure was effected only after abortion. One other patient, who had recurrent positive cultures after delivery was cured when treated post partum. In Table VIII, a comparison is made of the efficacy of therapy in pregnant and nonpregnant patients.

TABLE VII. EFFECT OF SUBSEQUENT TREATMENT OF PATIENTS WHO FAILED TO RESPOND TO INITIAL THERAPY

SULFANILAMIDE	SULFAPYRIDINE	SULFATHIAZOLE	SULFADIAZINE
22 cases	9 cases	6 cases	1 case
3 delinquent	1 delinquent	1 cured with sul-	1 cured with
7 cured with sulfapyri-	6 cured with sulfa-	fapyridine	sulfathi-
dine	thiazole	5 cured with sul-	azole
1 delinquent with sulfa-	1 delinquent with	fathiazole	
pyridine	sulfathiazole		
3 failures with sulfapy-	1 failure with sulfa-		
ridine but cured	thiazole but		
with sulfathiazole	cured with sulfa-		
7 cured with sulfathia-	diazine		
zole			
1 delinquent. Failure			
with both sulfapy-			
ridine and sulfathi-			
azole			

TABLE VIII. COMPARISON OF EFFICACY OF SULFONAMIDE THERAPY IN GONOCOCCAL INFECTION OF PREGNANT AND NONPREGNANT WOMEN

	NONPREGNANT			PREGNANT		
	TOTAL NO.	NO. FAILURES	%	TOTAL NO.	NO. FAILURES	%
Sulfanilamide	116	18	16	7	4	57
Sulfapyridine	148	6	4	11	3	27
Sulfathiazole	177	4	2	32	2	6
Sulfadiazine	111	1	0.9	11	0	0
Totals	552	29	5	61	9	15

Seventy per cent of the patients were seen post partum. None of their infants developed the infection, and none of them seemed to have been adversely affected by the treatment during pregnancy.

Course of Infection.—The infection was acute in 74 per cent of the patients, and of these 18 per cent had on the initial visit or developed subsequently salpingo-oophoritis or Bartholinitis. Of the 26 per cent of patients who had chronic infections, 20 per cent had these complications. Only 6 (16 per cent) of the 38 initial drug failures were in patients with chronic infections, while 8 (21 per cent) were in patients with acute infections with extensions. Seventeen per cent of the patients were asymptomatic except for a very slight discharge.

Time of Response to Therapy.—All but 3 per cent of the patients who responded to initial therapy had negative cultures the first visit 3 to 6 days after institution of therapy. Of the 38 failures, 22 (58 per cent), 5 of whom were pregnant, had positive cultures throughout treatment. Seventeen of the patients had been given sulfanilamide, 3 sulfapyridine, 1 sulfathiazole and 1 sulfadiazine; that is, 77 per cent of the initial sulfanilamide failures, 33 per cent of the sulfapyridine, 16 per cent of the sulfathiazole and 100 per cent of the sulfadiazine (only 1) failures did not respond to therapy even during treatment. Sixteen other patients became negative during treatment but relapsed later. Four of them were pregnant; in 2, positive cultures first occurred after termination (1 abortion, 1 term delivery). Of the 12 patients who menstruated, 10 had positive cultures within two months. The two exceptions were in a group of 235 patients reported earlier³ who had been observed three months. They both became delinquent before we could ascertain whether reinfection had occurred.

Provocative Test.—All the menaemic patients were given a provocative test of silver nitrate on the first or second postmenstrual day. Cultures were taken just preceding the instillation of silver nitrate and on the first and fourth day following it. Not all patients were able to return for cultures at the correct intervals, but all had at least one com-

plete provocative test before they were discharged. Many patients had two and a few had three completed tests. As has been stated previously, 9 out of 45 of the initial drug failures were in pregnant patients. Of the remaining 36 patients, 17 were shown to have positive cultures throughout treatment and 12 responded during treatment but subsequently became positive. In the last 7 patients of the failure group, the positive cultures occurred during or just following the menstrual period, and one became positive during the provocative test although negative cultures had been obtained postmenstrually. Menstrual or postmenstrual cultures, therefore, gave valuable information concerning cure in 7 of 12 (57 per cent) of the patients who relapsed after an initial response to therapy. Additional information was obtained in only one instance by the provocative test.

Previously, we had reported that if the provocative test were used as criteria of cure, cultures taken on the fourth day after instillation of the silver nitrate were more reliable than those taken on the first day following it. This conclusion was based on the fact that 8 patients who had positive cultures on the fourth day, had negative cultures postmenstrually, and on the first day following the use of silver nitrate. Further study showed that in every instance these patients had been reinfected.

In an attempt to evaluate better the provocative test, 25 patients who had positive cultures postmenstrually were treated with silver nitrate. Thirteen of them had positive cultures both the first and fourth day following its instillation; 4 had positive cultures the first day, but negative cultures the fourth day; 4 had negative cultures the first day, but positive cultures the fourth day; and 4 had negative cultures on both the first and fourth days. It would seem that the most reliable provocative test is the menstrual period itself.

Concentration of Hemoglobin and Drug.—Hemoglobin determinations* were made on all the patients before and after therapy was instituted in order to determine whether those with anemia responded differently to therapy, and what the effect of therapy was on hemoglobin concentration. Only five of the initial drug failures were in patients whose hemoglobin levels were below 70 per cent, whereas 13 were in patients with hemoglobin concentrations of over 90 per cent. About 20 per cent of the patients showed a slight decrease in hemoglobin after therapy. Only two patients showed an appreciable anemia.

Specimens of blood for determination of concentration of drug in the blood were taken once or twice during therapy. Concentrations as high as 10 mg. per 100 c.c. were obtained in patients who received sulfanilamide, but most of them were between 3 and 4 mg. per 100 cubic centimeters. With sulfapyridine and sulfathiazole, the highest levels were 8 mg. per 100 c.c., most of them being between 2 and 3 milligrams. With a 2-Gm. daily dose of sulfadiazine, the concentration of drug in the blood was usually 4 to 6 mg. per 100 cubic centimeters. Earlier, when a 3-Gm. daily dose was used, levels between 8 and 11 mg. per 100 c.c. were frequent. These seemed unnecessarily high and could be dangerous in ambulatory patients. For that reason, the daily dose was lowered to 2 Gm. with no resulting increase in failure of therapy. None of the patients who failed to respond to therapy had abnormally low concentrations of drug in the blood.

Toxicity.—A large number of the patients who received sulfanilamide and sulfapyridine exhibited minor toxic symptoms. The number of toxic symptoms was about as great with sulfadiazine as with sulfathiazole, but both drugs were tolerated better than sulfanilamide or sulfapyridine. Rarely was it necessary to discontinue therapy because of toxic symptoms.

*A carbon monoxide method was used for many tests while the Dare method was used for the rest of tests.

Discussion

In this investigation, 575 women in whom diagnosis and cure of gonococcal infection were based on cultural studies were treated with sulfanilamide, sulfapyridine, sulfathiazole or sulfadiazine. Of these, 51 were pregnant. Seventeen per cent of the patients were asymptomatic except for a slight discharge. The infection was acute in 74 per cent of the cases, and of these, 18 per cent either already had or later developed salpingitis or Bartholin's abscesses. Meanwhile, 20 per cent of the patients with chronic infections had or developed the same complications.

To the best of our knowledge, 101 patients were exposed to one or more infections and became reinfected during the period of observation following treatment; 37 were retreated with the same drug and 64 were given different drugs.

Of the 44 patients who failed to respond to one course of treatment, six responded to repeated courses of the same drug, four became delinquent following one course of therapy while still infectious, 27 were cured by a second drug, and two became delinquent following the second course of treatment. Five patients required more than two drugs. Drug-fast strains of gonococci were thus encountered occasionally.

Sulfadiazine was the drug of choice. With it 94 per cent were cured, with sulfathiazole 87 per cent, with sulfapyridine 82 per cent, and with sulfanilamide 71 per cent. If the patients who were exposed to reinfection were deleted and only failures to initial therapy were considered, the percentage failure with sulfadiazine was 1 per cent, with sulfathiazole 3 per cent, with sulfapyridine 6 per cent and with sulfanilamide 17 per cent. We believe that the low percentage of failures in our group was dependent somewhat upon an optimum dosage. Patients were better able to tolerate small amounts of the drug; and thus, they were more willing to take the drug and also better able to retain it, than when large doses were given.

A careful scrutiny of the patients who failed to respond to initial therapy revealed considerable information. Chronic infections responded to treatment as readily as did acute ones. Twenty-six per cent of the patients had chronic infections, while only 6 (16 per cent) of the 38 patients, who failed to respond to one drug, had chronic infection. Patients with secondary complications responded about as well as did other acute cases. Eighteen per cent of those with acute infections had secondary complications; 8 or 21 per cent of the failures were in cases with secondary complications.

Infection in the pregnant patient was more resistant to sulfonamide therapy than in the nonpregnant patient. Eighteen per cent of the failures were in patients who were pregnant, whereas the pregnant patients comprised only about 9 per cent (51 of 575 patients) of the whole series. The failure rate for the whole series was only 7 per cent (38 of 575). Three of the gravid patients did not respond to treatment until the late puerperium. Not one of the infants developed the infection, and except for the routine instillation of silver nitrate into the conjunctival sac, no other prophylactic measures were used. Not one of the infants seemed to be adversely affected by the treatment during pregnancy.

Ninety-seven per cent of the patients who responded to initial therapy had negative cultures before completion of the course of treatment, whereas 58 per cent of the patients who failed to respond to therapy had positive cultures throughout the course of treatment. Sixteen patients (2.7 per cent of the total number of patients treated) responded to therapy during treatment but later relapsed; 4 of them were pregnant. Of the remaining 12, 7 (57 per cent) had recurrent positive cultures during or just following the menstrual period. One had positive cultures during the menstrual period but did not return for a postmenstrual visit. The other five did not report for observation during the menstrual period. Most patients objected so strongly to visits during the menstrual period, that it was difficult to collect data on cultures during this time. Four of the patients had their first positive cultures following treatment and after the next menstrual period, 2 after the second menstrual period and one after the third menstrual period.

Three patients had relapses before the first menstrual period and one between the first and second menstrual period. One patient was cured only after the cervix had been cauterized.

Only one patient had negative cultures following the menstrual period, but had positive cultures following the provocative test. Since 12 of 25 patients who were given provocative tests when postmenstrual cultures were positive had negative cultures on either the first and/or fourth days after instillation of the silver nitrate, we believe the most reliable provocative test to be the menstrual period itself. No patient should be discharged without negative cultures following one menstrual period and preferably two. Two months' observation with continuous negative cultures and smears following cessation of therapy is sufficiently long in nearly all cases. Of the patients who responded to therapy and later relapsed, less than 1 per cent relapsed after the first month of observation.

Conclusions

1. Sulfadiazine is the drug of choice in the treatment of gonococcal infection in women. Sulfathiazole is slightly less effective. Both drugs gave better results and were better tolerated by the patients, than were sulfanilamide or sulfapyridine.

2. Diagnosis of gonorrhea and criteria of cure, wherever possible, should be based on cultural studies. Patients should be observed through at least one negative menstrual period and preferably two. Negative smears and cultures taken just following the menstrual period should be required. Considerable information is obtained from cultures taken during therapy.

3. The menstrual period is the best provocative test.

4. Complications of salpingitis or Bartholinitis were not associated with more failures of therapy than acute uncomplicated cases.

5. Drug-fast strains were produced in the adult women in less than 1 per cent of the cases.

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References

- Hesseltine, H. C., Hac, L. R., Adair, F. L., and Hibbs, D. K.: *Am. J. Syph. Gonorr. & Ven. Dis.* 25: 454, 1941.
2. Hac, L. R., Hesseltine, H. C., Adair, F. L., and Hibbs, D. K.: *AM. J. OBST. & GYNEC.* 41: 98, 1941.
3. Adair, F. L., and Hac, L. R.: *New England J. Med.* 227: 465, 1942.

EXERCISES IN DYSMENORRHEA

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ALTHOUGH a great deal of discrepancy exists in the literature with regard to the reported incidence of dysmenorrhea,* no one questions the actual gravity of this widespread ailment. Due to the untold suffering it causes to innumerable women, as well as to its obscure etiology, and the discouraging results of therapy, it constitutes one of the most refractory conditions in gynecology.

Moreover, there is another side to this problem besides the purely medical one, for, owing to the incapacitating effect of dysmenorrhea on large numbers of women in industry, its economic aspect is of tremendous importance. A compilation of sixteen reports on the subject shows that 45.5 per cent of women in childbearing age suffer from dysmenorrhea to some degree, and that 16.6 per cent are seriously handicapped during their menstrual periods.

These percentages may be translated in terms of actual economic loss. Figures derived from the 1940 census of the United States reveal that there are in this country about 32 million females, between 15 and 50 years of age. If 16.6 per cent of them, or about 5.3 million, have severe dysmenorrhea, and if one conservatively estimates two hours per period (for thirteen periods during the year, or a total of 26 hours yearly)† as the average length of time during which a member of this group is incapacitated, one can say roughly that 140 million hours are lost annually, due to this cause. The magnitude of this wastage is realized when one considers that, on the basis of a norm of 2,400 working hours a year per person (300 eight-hour working days), this loss of time represents an entire year of work by approximately 58,000 women!

*These range from Emge's¹ figure of 2.8 per cent for primary dysmenorrhea, to Lakeman's² statement that 89.6 per cent of industrial workers at some time, in some degree, experience pain during the menstrual period.

†In contrast to this figure, absenteeism from work due to that much publicized timewaster, the common cold, has been estimated, by the most reliable authority available³, to be on an average, one day (eight hours) a year per worker. Hence, within the group of severe dysmenorrheics, which constitutes one-sixth of the female population of childbearing age in the United States, the economic loss due to menstrual pain is more than three times that resulting from the common cold.

Furthermore, not only the actual absence from work must be taken into account, but one should also consider the innumerable hours lost to inefficiency when a woman is in pain during her menstrual period. This problem is of particular significance today because of the vast numbers of women engaged in our war industry. The possible grave results of a slip along the assembly line due to inattention, while a woman is in pain, need not be elaborated upon. Clearly, it would be a definite advance, both from a medical and from an economic standpoint, to have this great cause of loss of production removed from the factory, especially at this stage of the war effort.

In view of the gravity of this condition, it is not surprising that numerous investigators have devoted their time to this study. Various explanations have been given for the origin of this ailment, and many types of treatment have been resorted to in attempts to relieve it. The factors proposed at one time or another as possible etiologic agents, include mechanical, psychogenic, neurogenic, metabolic, allergic and constitutional ones. On the basis of the work of Ayer⁴ and Ussher,⁵ Billig⁶ emphasized the role of fascia contractions in dysmenorrhea, and suggested stretching exercises to correct this condition.

The system of exercises to be described in the present report has shown beneficial results, particularly in the primary form of this ailment.

Selection of Cases

The group studied consisted of 129 females between the ages of 15 and 37 years. The average age of the patient was 21.6 years, and the average age at menarche was 12.8 years. The subjects of the investigation included patients from the general gynecologic clinic at the Free Hospital for Women, as well as nurses and maids employed by the hospital. The remainder of the group was made up of students from Wellesley, Radcliffe, and Simmons Colleges, and patients from the writer's private practice in San Francisco. On the basis of clinical history, the group, as a whole, was divided into two parts: (1) primary dysmenorrhea, and (2) secondary dysmenorrhea.

Before proceeding further, it would be advisable to define our terms. *Primary* dysmenorrhea presents a fairly definite picture which has been used as a criterion for this study. The pain begins at menarche, or within 3 or 4 years thereafter, in girls of no one particular body build. The discomfort starts several hours to two or three days before the onset of catamenia in the form of cramplike or colicky pains, which are most severe in the lower midabdomen; the pain may radiate down along the thighs or to the lumbosacral region. It is often accompanied by nausea and vomiting, as well as by general malaise, and often a cold and clammy sensation of the hands and feet.

Under *secondary* dysmenorrhea, the writer would classify various other bizarre symptom complexes of which women complain, where pelvic pathology is likewise absent, but where the pains do not conform to the standards set down under primary dysmenorrhea.

We must also establish a criterion as to what is severe pain. Since we base our grading of pain on the word of the patient, the subjective element and psychogenic factors are bound to enter into our evaluation of the pain. If, however, we use the same basis for all the variations, such as pain threshold, neuroses, previous training, etc., these should balance each other. Individuals may vary with respect to their pain threshold,⁷ but it is the effect, not the stimulus, that is of consequence to the patient.

Our criteria for grading pain are as follows:

Severe Dysmenorrhea: When the patient is forced to bed during her menstrual period.

Moderate Dysmenorrhea: When the patient is forced to take some medication for relief, but is not confined to bed.

Mild Dysmenorrhea: When the discomfort is not severe enough to warrant medication.

Only those patients complaining of severe dysmenorrhea were included in the series.

Description of Exercises

The exercises, which have been devised for the relief of dysmenorrhea, are very simple to perform; they take less than five minutes a day, and require a minimum of space; they may be done at home, and need be carried out usually for only two or three months before improvement results.

These exercises may best be understood by referring to the charts which show the various positions assumed by the subject:

Position 1.—The patient stands at right angles to the wall at such a distance as will enable her to comfortably rest her left elbow on the wall on a level with her shoulder (Fig. 1*A* and *B*). The pelvis is tilted forward (Fig. 2*A* and *B*), and, while in this position, the patient touches the wall with her hip, keeping her knees straight (Fig. 3). Care must be taken not to twist the body, or allow the elbow to slide up or down along the wall.

Position 2.—The same procedure is repeated using the right elbow.

Position 3.—The patient faces the wall against which she rests both elbows (Fig. 4*A*). The pelvis is tilted (Fig. 4*B*), and the patient stretches until her pelvis touches the wall (Fig. 4*C*). The heels remain on the floor and the knees are kept straight.

Each position is assumed three times, and all are repeated three times a day. If, at the end of two or three months, sufficient relief is obtained, the exercises are discontinued for one or two months. Some patients have no recurrence of pain at catamenia; in others, where relapse occurs, the exercises are performed once daily for one week before the period is due, as a prophylactic measure. The patients were followed for two to twenty cycles after they started doing the exercises, the average being 6.5 cycles.

Results

As shown in Table I, the results are listed under three headings.

Satisfactory relief: Where the patient experienced 75 to 100 per cent relief from her pain and discomfort.

Partial relief: 25 to 75 per cent improvement.

No relief: 0 to 25 per cent improvement.

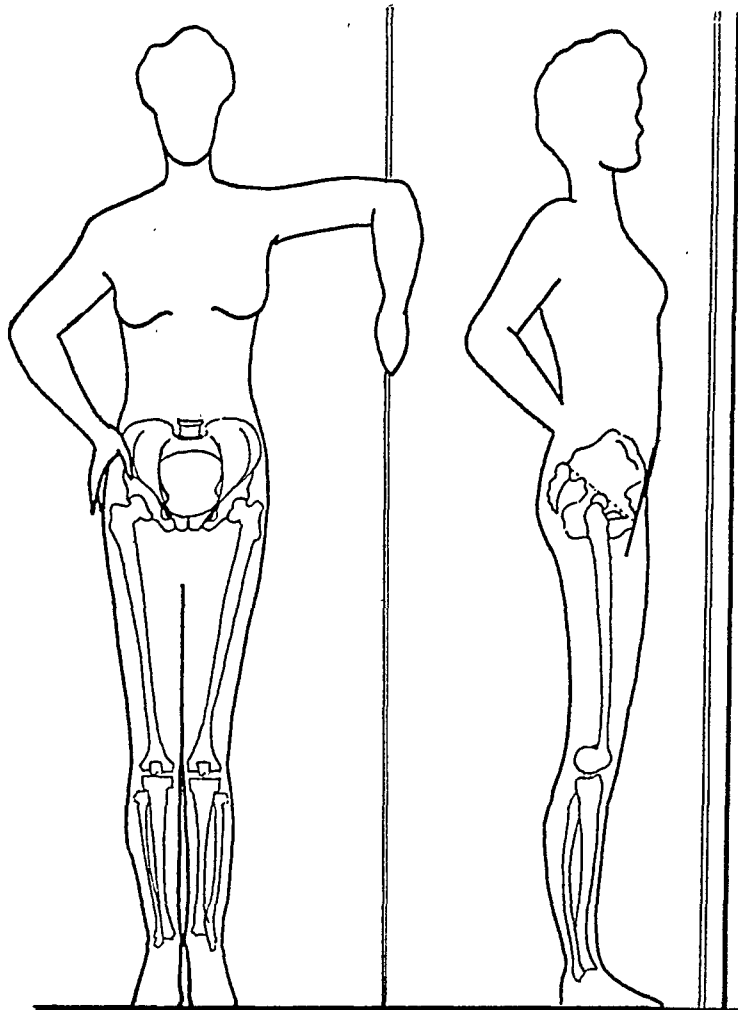
TABLE I

	PRIMARY DYSMENORRHEA		SECONDARY DYSMENORRHEA		TOTAL	
	NO. OF CASES	PER CENT RELIEVED	NO. OF CASES	PER CENT RELIEVED	NO. OF CASES	PER CENT RELIEVED
Satisfactory	64	76.2	31	68.9	95	73.6
Partial	11	13.1	3	6.7	14	10.9
Total	75	89.3	34	75.6	109	84.5
No relief	9	10.7	11	24.4	20	15.5

There was at least some degree of relief in nearly 85 per cent of the total series of patients treated. If we consider only those suffering from the primary form of dysmenorrhea, the percentage of relief was 89.3 per cent.

Discussion

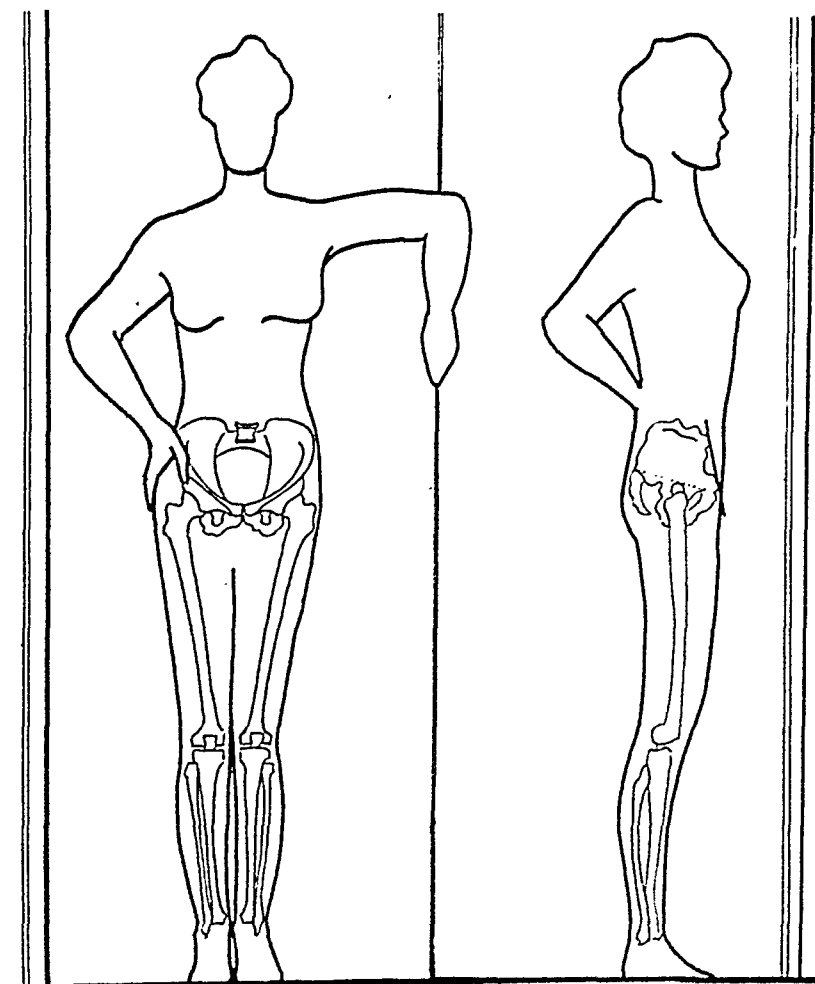
This figure of nearly 90 per cent compares very favorably with the results ascribed to other forms of therapy. These range from 65 per



A.

Fig. 1.

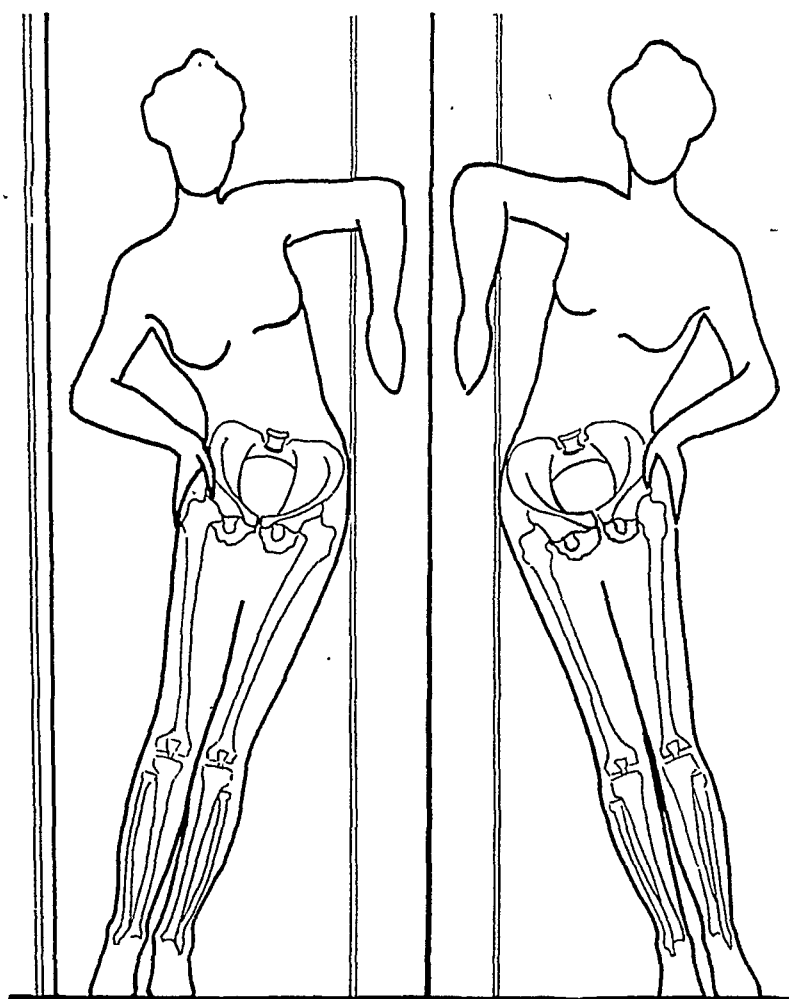
B.



A.

Fig. 2.

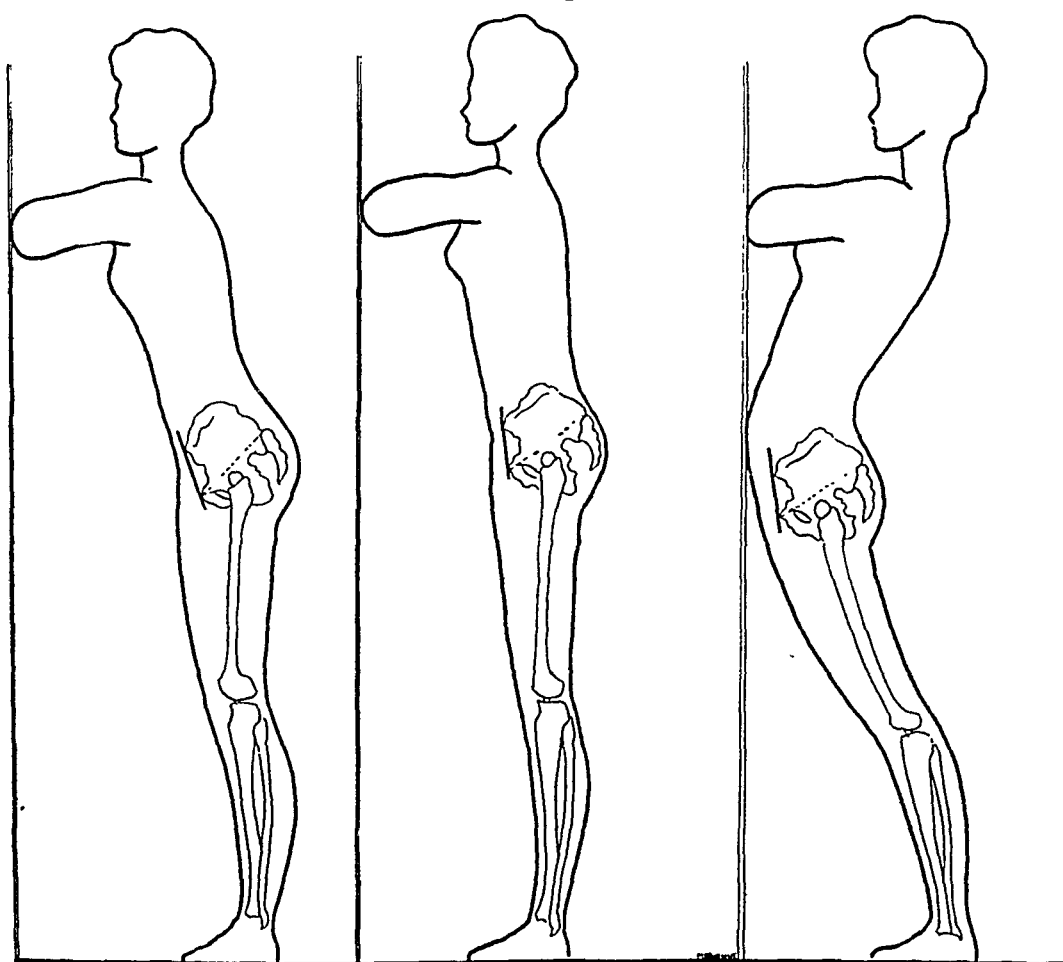
B.



A.

Fig. 3.

B.



A.

B.

C.

Fig. 4.

cent, where benzedrine was reported to constitute the alleviatory agent,⁸ to 95 per cent, allegedly achieved by the combination of x-ray and Antuitrin-S.⁹ This latter degree of success has also been reported by resorting to psychotherapy.¹⁰ Other measures, reputed to yield intermediate percentages of cure or relief, include the use of hormones,^{9, 11-21} dietary regulation,^{11, 21, 22} surgical or mechanical procedures,²³⁻³⁰ and even treatment of allergy.³¹⁻³⁴ Each of these forms of therapy has been claimed by its respective proponent to cure more than half of the cases treated. However, many of the series studied were small, the number of patients ranging from 5 to 60. At present, the word "cure" applied to dysmenorrhea denotes a cure similar to that for diabetes or hyperthyroidism, a substitution therapy. This is unfortunately true of most drugs and hormones that have been used in attempts to alleviate this condition.

Furthermore, in evaluating these percentages of "cure," one should bear in mind the statement of Ehrenfest:³⁵

"Reading the immense literature on dysmenorrhea, mostly extolling results with this or that therapy, one cannot fail to be impressed by the tendency of writers to fall into deceptive *post hoc ergo propter hoc* reasoning. Many writers appreciate the important role played by suggestion in the seeming efficacy of any therapeutic measure applied to a woman in a highly nervous and emotional state while suffering pain."

Up to the present time, mechanical methods, such as dilatation of the cervix, presacral resection, or exercises, seem to offer the best and most lasting cures. The exercises described here are much simpler to perform than those reported by previous writers;³⁶⁻⁴⁰ they entail little time and no expense; and in many cases, the beneficial results have lasted for at least twenty months, which was the limit of the follow-up period in this investigation.

Summary

In a group of 129 dysmenorrheics, of whom 84 suffered from primary dysmenorrhea, and 45 from secondary dysmenorrhea, treatment by special exercises was followed by definite relief in 84.5 per cent of the cases. In many instances, the beneficial effect lasted for at least twenty-months, which was the limit of the follow-up period in this investigation. Within the subgroup of those afflicted with primary dysmenorrhea, the percentage of alleviation was 89.3.

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References

1. Emge, L. A.: The Problem of Dysmenorrhea, California & West. Med. 39: 380-385, 1933.
2. Lakeman, M. R.: Menstrual Pain Among Industrial Women, New England J. Med. 209: 237-239, 1933.
3. Lanza, A. J.: Incidence and Costs of Acute Respiratory Disease in Industry, J. A. M. A. 116: 1342-1343, 1941.
4. Ayer, J. B.: Clinical Neurology, New England J. Med. 223: 376-380, 1940.
5. Ussher, N. T.: The Viscerospinal Syndrome—A New Concept of Visceromotor and Sensory Changes in Relation to Deranged Spinal Structures, Ann. Int. Med. 13: 2057-2090, 1940.
6. Billig, H. E.: Back Pain and Neuritis, Clin. Med. 48: 96-99, 1941.
7. Haman, J. O.: Pain Threshold in Dysmenorrhea, AM. J. OBST. & GYNEC. 47: 686-691, 1944.

8. Larkin, W. J.: A Survey of Dysmenorrhea in a Group of Student Nurses and the Medical Treatment by Means of Benzedrine Sulfate, *Pennsylvania M. J.* 44: 994-997, 1941.
9. Kotz, J., and Parker, E.: Primary Dysmenorrhea, An Endocrine Problem, *Am. J. Obst. & Gynec.* 34: 38-46, 1937.
10. Johnstone, R. W.: Dysmenorrhea, *Edinburgh M. J.* 47: 1-15, 1940.
11. Altschul, A.: The Treatment of Dysmenorrhea With Insulin. (Preliminary Report), *J. A. M. A.* 106: 1380-1383, 1936.
12. Campbell, R. E., and Hisaw, F. L.: The Use of Corpus Luteum in the Treatment of Dysmenorrhea, *Am. J. Obst. & Gynec.* 31: 508-510, 1936.
13. Elden, C. A., and Wilson, K. M.: The Progesterone Treatment for Dysmenorrhea, *Am. J. Obst. & Gynec.* 32: 91-96, 1939.
14. Sturgis, S. H.: The Use of Stilbestrol in the Relief of Essential Dysmenorrhea, *New England J. Med.* 226: 371-376, 1942.
15. Hamblen, E. C.: Rationale of Androgenic Therapy in Gynecology, *J. Clin. Endocrinol.* 1: 180-186, 1941.
16. Browne, W. H.: The Use of Follutein in Dysmenorrhea, *Am. J. Obst. & Gynec.* 29: 113-116, 1935.
17. Goldberg, M. B., and Lisser, H.: On the Clinical Use of Emmenin (Human Placental Extract—Collip), *Endocrinology* 19: 649-655, 1935.
18. Rubinstein, H. S., and Abarbanel, A. R.: The Use of Testosterone Propionate in the Treatment of Dysmenorrhea, *Am. J. Obst. & Gynec.* 37: 709-715, 1939.
19. Cinberg, B. L.: Androgens in the Treatment of Dysmenorrhea, *New York State J. Med.* 42: 2138-2141, 1942.
20. Hirst, D. V., Hamblen, E. C., and Cuyler, W. K.: Rationale of Estrogenic Therapy in Functional Dysmenorrhea, *J. Clin. Endocrinol.* 2: 442-446, 1942.
21. Schrick, E. W.: Insulin Treatment of Dysmenorrhea, *Am. J. Obst. & Gynec.* 37: 146-147, 1939.
22. Tedstrom, M. K., and Wilson, L. E.: Menstrual Hypoglycemia and Functional Dysmenorrhea: Their Relationship, *California & West. Med.* 44: 375-381, 1936.
23. Cannon, D. J.: Modern Theories of Dysmenorrhea, *J. Obst. & Gynaec. Brit. Emp.* 43: 492-506, 1936.
24. Weir, W. H.: Results With the Intrauterine Stem Pessary, *Am. J. Obst. & Gynec.* 33: 291-299, 1937.
25. Sears, N. P.: The Relation of Ureteral Pain to Menstruation, *Am. J. Obst. & Gynec.* 37: 685-689, 1939.
26. *Proc. Roy. Soc. Med.*: Discussion on Intrinsic Dysmenorrhea 29: 931-953, 1936.
27. Younge, P.: Personal communication.
28. Shaw, W.: The Treatment of Spasmodic Dysmenorrhea, *Lancet* 2: 143, 1933.
29. Sellers, T. B.: Pain Associated With Menstruation, *Southern M. J.* 25: 167-175, 1932.
30. Larkin, W. J.: An Office Procedure for the Treatment of Primary Dysmenorrhea, *Pennsylvania M. J.* 41: 348-354, 1938.
31. Rowe, A. H.: Uterine Allergy, *Am. J. Obst. & Gynec.* 24: 333-338, 1932.
32. Schwarz, O. H., and Smith, D. R.: Essential Dysmenorrhea and Allergy, *Am. J. Obst. & Gynec.* 33: 331-336, 1937.
33. Dutta, P. C.: Allergy and Dysmenorrhea, *J. Obst. & Gynaec. Brit. Emp.* 42: 309-317, 1935.
34. Duke, W. W.: Allergy, Asthma, Hay Fever, Urticaria and Allied Manifestations, St. Louis, 1926, The C. V. Mosby Co.
35. Ehrenfest, H.: Menstruation and Its Disorders. A Critical Review of the Literature From 1933 to 1936 Inclusive, *Am. J. Obst. & Gynec.* 34: 699-729, 1937.
36. Ewing, R. E.: A Study of Dysmenorrhea at the Home Office of the Metropolitan Life Insurance Company, *J. Indust. Hyg.* 13: 244-251, 1931.
37. Clow, A. E. S.: Treatment of Dysmenorrhea by Exercise, *Brit. M. J.* 1: 4-5, 1932.
38. Bell, M., and Parsons, B.: Dysmenorrhea in College Women, *M. Woman's J.* 38: 31-35, 1931.
39. Stevenson, A. D.: The Treatment of Dysmenorrhea, *Lancet* 2: 599, 1938.
40. Adams, T. W.: Painful Menstruation. With Especial Reference to Posture as and Etiologic Factor, *West. J. Surg.* 42: 88-89, 1934.

THERAPEUTIC INTERRUPTION OF PREGNANCY

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THIS report, which is based upon the experience of The New York Lying-in Hospital from September, 1932, through December, 1943, concerns 280 pregnancies which were interrupted for therapeutic reasons. The vast majority of these, 233 or 83.2 per cent represent what are commonly termed therapeutic abortions, i. e., performed prior to the sixteenth week of pregnancy, but the inclusion of all interruptions prior to viability of the infant, which we have limited to 1,500 grams, broadens our scope. Two hundred and twenty-two, or 79.3 per cent, were clinic patients, while the remaining 58, or 20.7 per cent were performed by private physicians. During this period, 46,861 pregnant women were treated, hence the incidence of therapeutic interruption is 0.6 per cent. On the average, 23.3 interruptions were performed each year.

There were 44 indications for interruption which may be grouped under nine major headings as shown in Table I.

As illustrated, toxemia and cardiac disease accounted for 58.2 per cent, or almost three-fifths of all the interruptions.

TABLE I.—INDICATIONS

GROUP	NUMBER OF CASES	PERCENTAGE
Toxemia	97	34.6
Cardiac disease	66	23.6
Pulmonary disease	31	11.1
Urologic disease	27	9.6
Neurologic and psychiatric disease	16	5.7
Medical diseases	14	5.0
Obstetric complications	10	3.6
Gynecologic complications	10	3.6
Miscellaneous	9	3.2
	280	100.0

TABLE II.—TOXEMIA

TYPE	NUMBER OF CASES
Renal disease	56
Acute glomerulonephritis	4
Hypertensive disease	21
Severe Pre-eclampsia	8
Eclampsia	3
Previous toxemia	5
Total	97

In Table II, it is evident that renal disease was the type of toxemia most frequently encountered. The patients were usually grand multiparas and gave evidence of their disease by persistent albuminuria and impairment of renal function. In the four pregnancies which were complicated by acute nephritis, the pregnancy was interrupted to avoid

strain on the kidneys during this acute phase, and the decision regarding future pregnancies was dependent upon the development of chronic nephritis. Severe pre-eclampsia and eclampsia, as would be expected, led to interruption in the later months of pregnancy. The five cases, in which previous toxemia was the indication, were instances in which no disease was present at the time of interruption, but where the interruption closely followed a pregnancy complicated by severe pre-eclampsia.

All but four of the therapeutic interruptions based on cardiac indications were performed for rheumatic heart disease. The majority of these patients belonged to Class III of the New York Heart Association Classification, while a few were Class IV. Of the remaining four, two were performed because of congenital heart disease, while the other two interruptions occurred in the same individual who had constrictive pericarditis. Twenty-seven of the 31 interrupted on the basis of pulmonary disease were done because of tuberculosis, two were done because of the bronchiectasis, one because of chronic bronchitis, and one because of allergic rhinitis. This last patient already had had two children who had asthma.

Twenty-one interruptions were performed because of pyeloureteritis; sixteen of these were performed during the period from 1932 through 1938, while only five were performed during the second half which ended in 1943. The advent of sulfamilamide and its derivatives has rendered almost unnecessary the interruption of pregnancy because of intractable pyeloureteritis. This is in striking contrast to a decade ago, when pregnancies frequently had to be interrupted, and even despite this, chronic renal infection often resulted. Of the five pregnancies which were interrupted because of pyeloureteritis during the past five years, one of these was complicated by renal tuberculosis and another by sulfanilamide sensitivity. Three of the pregnancies which were interrupted on urological grounds occurred in patients with one kidney—one patient had had a previous nephrectomy for an aneurysm of the right renal artery, and now had hypertension with the blood pressure ranging around 230/110; the second had had a nephrectomy because of renal stone, the third because of renal tuberculosis; these last two patients had infections due to *B. coli* in the remaining kidney.

Six of the fourteen interruptions performed for medical reasons were done because of hyperthyroidism; two of these were performed in the same individual, a girl seventeen years of age, who had had three thyroidectomies in the course of three years. Two were done because of Hodgkin's disease; one was performed because of ulcerative colitis which had resulted in invalidism. Of the sixteen pregnancies which were interrupted for neurologic and psychiatric reasons, nine were performed in patients with psychosis, which was usually manic-depressive in type. While it is not our usual practice to interrupt pregnancies because of epilepsy, three such interruptions were done because of extenuating circumstances. Three interruptions were performed because of far-advanced multiple sclerosis involving the legs and the bladder; patients with less severe grades of multiple sclerosis were permitted to go to term.

Vomiting of pregnancy led to the interruption of seven pregnancies, all of which were performed prior to 1938. Since that time, because of the newer modes of therapy, e.g., intravenous glucose and parenteral vitamins, no pregnancy has had to be interrupted because of vomiting. Previous Watkin's interposition of the uterus led to the termination of two pregnancies, while the presence of ovarian carcinoma caused one pregnancy to be ended. Previous carcinoma, three in the breast and one in the stomach, also caused interruption of pregnancy. Three pregnancies were interrupted because of myomas, and one each because of repeated intrauterine fetal death, vesicovaginal fistula, scoliosis and spondylolisthesis.

Forty-four or 15.7 per cent of the pregnancies terminated were in the Negro race, while 236 or 84.3 per cent were in the white race.

TABLE III.—INDICATION IN THE NEGRO RACE

INDICATION	NUMBER OF CASES	PERCENTAGE
Renal disease	30	68.2
Hypertensive disease	6	13.5
Rheumatic heart disease	3	6.8
Congenital heart disease	1	2.3
Tuberculosis	1	2.3
Pyelonephritis	1	2.3
Severe pre-eclampsia	1	2.3
Myoma	1	2.3
Total	44	100.0

Renal disease is by far the leading reason for termination of pregnancy in the Negro race. Thirty or 53.6 per cent of the 56 patients with renal disease were Negroes, while 26 or 46.4 per cent were white. The Negro race constituted only 15.7 per cent of all the patients, but it represented 53.6 per cent of those with renal disease. From another view point, 68.2 per cent of the pregnancies in the Negro race were terminated because of renal disease, while only 11.2 per cent of the pregnancies in the white race were interrupted for this reason. The low incidence of interruption for tuberculosis and rheumatic heart disease is not because of the low incidence of these diseases in the Negro race, but rather because these patients go to municipal hospitals.

The greatest percentage of interruptions, 151 or 53.8 per cent, occurred in the period of greatest fertility, the decade between 25 and 35 years of age.

TABLE IV.—AGE

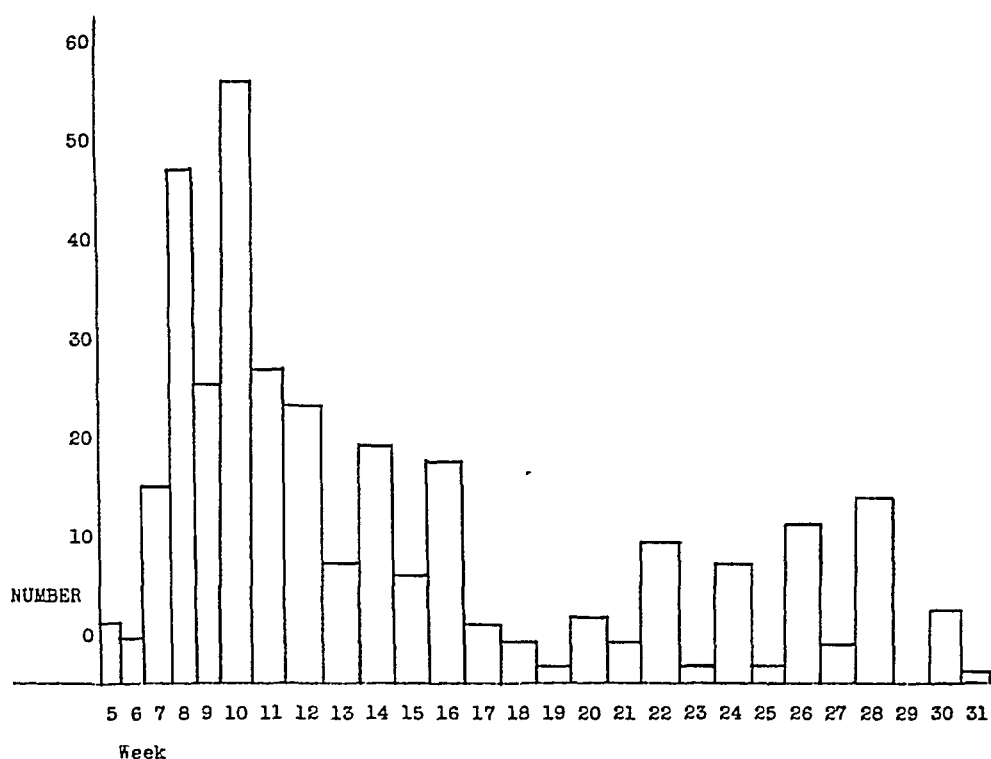
AGE GROUP	NUMBER OF CASES	PERCENTAGE
15 to 19	8	2.8
20 to 24	33	11.5
25 to 29	71	25.3
30 to 34	80	28.5
35 to 39	67	24.5
40 to 44	20	7.1
45 or over	1	0.3
Total	280	100.0

Discussion is required of only two groups, those over 45 and those under 20 years of age. Tuberculosis was the indication for the only pregnancy which was interrupted in a woman over 45 years of age.

In the group under 20, four were interrupted in early pregnancy, one because of rheumatic heart disease, one because of congenital heart disease, and two in the same individual because of hyperthyroidism; the other four were performed in late pregnancy, three for pyelitis and one because of eclampsia.

As is seen in Table V the greatest number of interruptions was in the tenth week as calculated from the last menstrual period.

TABLE V.—WEEK OF INTERRUPTION



Since it is assumed that conception usually occurs about two weeks after the last menses, the actual duration of pregnancy is obtained by subtracting two weeks. Two hundred and thirty-three, or 83.2 per cent of these interruptions were performed prior to the sixteenth week of pregnancy, and hence, constitute what are usually called therapeutic abortions. The remaining 47, or 16.8 per cent were performed after the sixteenth week of pregnancy for pre-eclampsia, eclampsia, pyeloureteritis, hypertensive disease, renal disease and occasionally cardiac disease.

At the time of the therapeutic interruption, 72 or 25.6 per cent of the patients had no living children, 75 or 26.3 per cent had one living child, 41 or 14.7 per cent had three living children, and the remaining 60 or 21.9 per cent had four or more children. Multiparity occasionally bolstered the indication in borderline cases. Grave, indeed, must be the indication which would warrant interruption of a first pregnancy. Table VI, which enumerates the indications for interruption of a first pregnancy, discounts the influence of parity. Interruption in the early weeks of a first pregnancy was usually performed in women who never should have become pregnant; termination in the later months is not so significant, and was usually performed for conditions such as severe pre-eclampsia and pyeloureteritis, which do not contraindicate further childbearing.

TABLE VI.—THERAPEUTIC INTERRUPTION IN THE FIRST PREGNANCY

INDICATION	NUM- BER OF CASES	AVER- AGE AGE	NEVER PREG- NANT AGAIN	SUBSEQUENT COURSE		TERM DELIVERY
				THERA- PEUTIC ABOR- TION	SPON- TANEOUS ABOR- TION	
Tuberculosis	10	27.1	9	0	9	1—3 yr. later
Pyeloureteritis	8	20.5	3	1—3 yr. later	0	1—3, 5, 8 yr. later
					1—2 yr. later	1—macerated infant 1 yr. later
Renal disease	6	23.5	6	0	0	1—3 yr. later
Rheumatic heart disease	5	29.0	5	0	0	0
Vomiting	3	28.0	2	0	0	1—2 yr. later
Eclampsia	2	20.5	0	0	0	1—macerated infant 1 yr. later
						1—5 yr. later
Severe pre- eclampsia	2	30.0	2	0	0	0
Myoma	2	31.5	2	0	0	0
Congenital heart disease	2	20.5	1	0	0	1—4 yr. later
Acute glomerulo- nephritis	2	21.5	1	1—4 yr. later	0	0
Scoliosis	1	27.0	0	0	0	1—3, 6 yr. later
Hypertensive disease	1	22.0	1	0	0	0
Bronchiectasis	1	27.0	1	0	0	0
Premature separa- tion of placenta	1	29.0	0	0	0	1—1 yr. later
Retinitis pig- mentosa	1	33.0	1	0	0	0
Multiple sclerosis	1	25.0	1	0	0	0
Hypertthyroidism	1	17.0	0	1—1 yr. later	2—2 yr. later	1—6 yr. later
Number	49		35	3		11
Percentage	100%		71.4%	6.1%		22.5%

The fact that 35 or 71.4 per cent of these patients never became pregnant again shows the imperativeness of interruption. Tuberculosis is first, resulting in 20 per cent of all the interruptions in the first pregnancy. Other diseases which manifest themselves in early life, such as congenital heart disease and acute glomerulonephritis, are also present.

When so serious a decision as the interruption of pregnancy is reached, the question arises whether pregnancies had ever been previously forbidden by a physician. In 100 or 35.7 per cent of our patients, pregnancy had been previously interdicted; in 78 or 27.9 per cent, it had not been forbidden, while in 102 or 36.4 per cent, no information is available. Sterilization had been performed in three of the cases in which pregnancy had occurred after its interdiction. This had been done by three different methods: (1) electrocoagulation of the tubes, (2) tubal resection by a vaginal route at the time of an interposition operation and, (3) abdominal tubal resection.

As is illustrated in Table VII, the majority of these interruptions were performed by the vaginal route.

The duration of pregnancy is the prime factor in the determination

TABLE VII.—METHOD OF INTERRUPTION

METHOD	NUMBER OF CASES		PERCENTAGE
<i>Vaginal Operation</i>	204	72.8	
One stage (dilatation and curettage)			
Without sterilization	108		38.5
With sterilization	27		9.7
Two stage (preliminary packing of cervix and curettage next day)			
Without sterilization	46		16.4
With sterilization	3		1.0
Hysterotomy	4		1.4
Bougie	1		0.3
Voorhees' bag	15		5.5
<i>Abdominal Operation</i>	76	27.2	
Without sterilization, hysterotomy	8		2.9
With sterilization, hysterectomy	19		6.8
Hysterectomy plus unilateral salpingo-oophorectomy	3		1.0
Hysterectomy plus bilateral salpingo-oophorectomy	1		0.3
Hysterotomy plus tubal sterilization	45		16.2
Total	280	100.0	

of the route of interruption. Occasionally, however, the intention of the operator to effectively end all childbearing leads to an hysterotomy and tubal ligation. Table VII is self-explanatory except in the instances where sterilization was not done though the pregnancy was terminated by an abdominal route, and the case in which both ovaries were removed in a young woman. The latter was done because of bilateral papillary serous cystadenocarcinoma. In the former eight cases, sterilization was not done in five patients in whom future childbearing was to be permitted (two patients with vomiting, two with severe pre-eclampsia and one with premature separation of the placenta); in two instances, in which legal involvements arising from illegitimacy were present; and in one case, in which sterilization was refused by the patient.

As illustrated in Table VIII, sterilization was performed in 98 cases or 35 per cent; 30 of these were done simultaneously with or shortly after a curettage, while 68 were performed at the time of laparotomy. In the majority of cases in which pregnancy was terminated, further childbearing was interdicted either temporarily or permanently.

TABLE VIII.—ATTITUDE TOWARD FUTURE PREGNANCIES

RECOMMENDATION	NUMBER OF CASES	PERCENTAGE	
Pregnancy interdicted	211	75.3	
Contraception		113	40.3
Sterilization (tubal ligation 72, hysterectomy 26)		98	35.0
Pregnancy not interdicted	11	3.9	
No preventive measures	7	2.6	
Unknown	51	18.2	
Total	280	100.0	

In Table VIII, future pregnancies were not interdicted in 11 patients—five of these had vomiting of pregnancy, two of these were unmarried, and one each had premature separation of the placenta, pyeloureteritis, severe pre-eclampsia and myasthenia gravis. Of the seven patients in whom no preventive measures were taken, three left the hospital against

advice, two refused sterilization or contraceptive advice, one died and one returned to her own physician. The group of which we are uncertain was largely composed of private patients, a large number of whom were undoubtedly given contraceptive advice later by their physician, though there is no mention of this in the record of their hospital stay. An analysis of the prevention of future childbearing reveals the fact that previous failure of contraception leads to sterilization after subsequent abortions and pregnancies.

The choice of anesthesia was influenced primarily, by the indication for operation (patients with pulmonary or cardiac complications usually receiving local anesthesia), and secondarily, by the preference of the surgeon.

TABLE IX.—ANESTHESIA

TYPE	NUMBER OF CASES	PERCENTAGE
<i>Total Inhalation</i>	157	56.0
Nitrous oxide and ether (95)		
Ether by open drop (30)		
Nitrous oxide (24)		
Cyclopropane (7)		
Ethylene (1)		
<i>Basal—Local</i>	102	36.4
<i>Avertin and Nitrous Oxide</i>	21	7.6
Total	280	100.0

In 13 or 6.4 per cent of the 204 pregnancies which were interrupted by a vaginal operation, the pregnancy was not terminated by the curettage; five expelled the fetus and one expelled part of the placenta subsequently, while in the remaining seven, a second curettage was necessary at intervals varying from two to eight weeks, and in each case degenerated decidua was obtained. In the five instances in which the fetus was expelled after the curettage, this occurred once on the first day, twice on the second day, once on the fourteenth day and once on the nineteenth day. In three instances or 1.5 per cent, the uterus was ruptured and a subtotal hysterectomy had to be performed. Only one bicornuate uterus was encountered, and in this patient, a cornual resection was done. Two ectopic pregnancies were found. In the first case, a left interstitial pregnancy was found during the performance of a sterilization eight days after the initial curettage. In the second instance, a left tubal pregnancy was found at a laparotomy performed because the curettage had shown only decidua and no chorionic elements.

Of the 204 patients who had a vaginal operation, 144 were afebrile, 25 had one day of fever, 26 had two or more days of fever due to intrauterine infection, while nine had two or more days of fever due to extrauterine causes. Nineteen of the 76 patients, who had laparotomies were afebrile, 23 had one day of fever, and the remaining 34 had two or more days of fever. In the group of vaginal cases with fever, a number of the patients also had an abdominal sterilization after the curettage, and hence, it is difficult to determine whether the fever is due to the vaginal manipulation, or to the laparotomy. There were no deaths as a result of infection in our series.

TABLE X.—SUBSEQUENT PREGNANCIES

A.—Allowed to Continue							
CASE	TIME INTER- VAL SINCE THERAPEUTIC ABORTION		CONTRA- CEPTION PREVI- OUSLY ADVISED	FUTURE CHILD- BEARING PERMA- NENTLY FOR- BIDDEN	COURSE		
	YR.	MO.			PRE- MATURE OR TERM DE- LIVERY	SPONTA- NEOUS ABOR- TION	STERILI- ZATION
1. Renal disease	1	0	Yes	Yes	+		+
2. Severe pre-eclampsia	4	0	No	No	+		
	6	0	No	No	+		
3. Severe pre-eclampsia	2	6	No	No	+		
4. Rheumatic heart	1	2	Yes	Yes	+		
disease	2	9	Yes	Yes	+		+
5. Congenital heart dis- ease	3	3	No	?	+		+
6. Pulmonary tubercu- losis	3	6	Yes	Tempo- rary (2 yr.)	+		
7. Pulmonary tubercu- losis	0	9	Yes	?		+	
	4	0	Yes	?	+		
8. Pyeloureteritis	2	2	Yes	No	+		
9. Pyeloureteritis	4	0	No	No		+	
	7	0	No	No	Dead macer- ated infant		
10. Pyeloureteritis	3	0	Yes	Yes	+		+
11. Pyeloureteritis	0	9	Yes	Yes	+		
12. Pyeloureteritis	3	0	?	No	+		
	5	0	No	No	+		
	9	0	No	No	+		
13. Pyeloureteritis	3	0	Yes	Tempo- rary (1 yr.)	+		
	6	0	No	No	+		
14. Hydronephrosis	3	6	Yes	Yes	+		+
15. Hyperthyroidism	2	9	Yes	Tempo- rary (1½ yr.)	+		
16. Hyperthyroidism	5	6	Yes	No	+		
17. Premature separation of placenta	1	6	No	No	+		
18. Scoliosis	3	0	Yes	No	+		
	6	0	No	No	+		+
19. Pregnancies in too close proximity	3	0	?	No	+		
Average time	3	8					
B.—Not Allowed to Continue							
CASE	INDICATION	TIME SINCE LAST INTERRUPTION		METHOD OF PREVENTION			
		YEAR	MONTH	PRIOR TO INTER- RUPTION CONTRA- CEPTION	AFTER INTERRUPTION		
					CONTRA- CEPTION	STERILI- ZATION	
I. Done Here							
20. Renal disease		0	10	+	+		
21. Renal disease		1	3	+			+
22. Renal disease		3	0	+			Refused
23. Hypertensive disease		2	0	+			+
24. Rheumatic heart disease		0	10	+	+		
25. Constrictive pericarditis		0	8	+	+		
26. Pyeloureteritis		3	0	?	+		
27. Pyeloureteritis		3	0	+			+
28. Psychosis		0	9	+	?		
29. Hyperthyroidism		0	5	+	+		
II. Done Elsewhere							
30. Acute glomerulonephritis		1	3	+	?		
Average time		1	6				

What is the obstetric history of patients after the interruption of a pregnancy? A partial answer is given in Table X.

In Table X, *A*, are represented 27 pregnancies, which occurred in 19 individuals. Five of these pregnancies were in four patients in whom the intention at the time of the therapeutic interruption was to end childbearing permanently; four of these individuals were subsequently sterilized. The remaining 22 pregnancies occurred in fifteen individuals in whom, despite the interruption of one pregnancy, it was thought that future pregnancies might be permitted. In the 38 pregnancies which followed therapeutic interruptions of pregnancy, 23 living children were born, two spontaneous abortions occurred, one macerated infant and one premature infant who died shortly after birth were delivered, and 11 pregnancies, as shown in Table X, *B*, were interrupted for the second time. Hence, eleven or 3.9 per cent. of the patients who had a previous therapeutic interruption here required a second termination of pregnancy. In addition, as illustrated in Table XI, 12 other patients, who had had a therapeutic interruption elsewhere, and three who had had two therapeutic interruptions elsewhere, required another termination of pregnancy for therapeutic reasons.

TABLE XI.—REPEAT THERAPEUTIC INTERRUPTIONS
(Only the last done at New York Hospital)

CASE	INDICATION	TIME SINCE LAST INTER- RUPTION		PREVENTION OF PREGNANCY		REMARKS
		YR.	MO.	PRIOR TO IN- TERRUPTION	AFTER IN- TERRUPTION	
1. Renal disease		2	0	?	Contracep- tion	
2. Renal disease		3	0	?	?	
3. Renal disease		6	0	?	Hysterectomy	
4. Rheumatic heart disease		6	0	?	?	
5. Rheumatic heart disease		1	0	?	?	
6. Rheumatic heart disease		7	0	Contracep- tion	Sterilization	
7. Rheumatic heart disease		4	0	Contracep- tion	Sterilization	
8. Rheumatic heart disease		5	0	?	?	
Rheumatic heart disease		3	0	?	?	3rd Thera- peutic in- terruption
9. Tuberculosis		3	0	?	?	
Tuberculosis		2	0	?	?	3rd Thera- peutic in- terruption
10. Tuberculosis		0	3	?	Sterilization	
11. Tuberculosis		4	0	?	Contracep- tion	
12. Chronic bronchitis		9	0	?	?	
13. Psychosis		13	0	?	?	
14. Vomiting		1	0	?	?	
15. Vomiting		11	0	Contracep- tion	Contracep- tion	
Vomiting		3	0	Contracep- tion	?	3rd Thera- peutic in- terruption

Tables X, *B* and XI show that 23 of our patients required a second therapeutic interruption, while three needed a third. In all, 29 repeat therapeutic interruptions were performed in 26 patients, an incidence of 10 per cent. The shortest time interval between the therapeutic interruptions was three months, the longest was 13 years, while the average was three and one-half years.

Frequently, the decision to interrupt a pregnancy can be reached only after grave deliberation. There is no question, however, but that the termination of a pregnancy is justifiable when the patient subsequently dies of the disease, which was the indication for the interruption. As illustrated in Table XII, there were thirteen such patients in this series. The majority of these were included in the earlier half of the study, 1932 to 1938, and hence, have been followed longer than those whose pregnancies were interrupted during 1938 through 1943.

TABLE XII.—DEATHS

CASE	INDICATION FOR INTERRUPTION	TIME SINCE THERAPEUTIC INTERRUPTION		CAUSE OF DEATH	POST MORTEM
		YR.	MO.		
<i>I. Cause of Death Same as the Indication for Therapeutic Interruption</i>					
1. Renal disease		0	3	Uremia	Not obtained
2. Renal disease		0	11	Uremia	Not obtained
3. Renal disease		2	2	B.P. was 260/160, N.P.N. was 91, two weeks prior to sudden death at home.	Not obtained
4. Renal disease		2	3	Sudden death	Not obtained
5. Renal disease		2	4	Sudden death	Not obtained
6. Renal disease		3	4	B.P. was 225/150, vision poor, urea clearance 10%, two months prior to sudden death.	Not obtained
7. Rheumatic heart disease			10 days	III C. Embolism of both iliac arteries with gangrene of left leg.	Not obtained
8. Rheumatic heart disease			21 days	Decompensation and fibrillation.	Mural thrombus of left auricle and renal infarcts.
9. Rheumatic heart disease		7	3	Class III C. Fibrillation	Endocarditis
10. Rheumatic heart disease		7	5	Class III C. Recurrent decompensation for 9 years.	Not obtained
11. Multiple sclerosis		0	4	Incontinent, could not stand.	Not obtained
12. Hodgkin's disease		1	3	Dyspnea due to lung infiltration	Involvement of lungs, liver, diaphragm, jejunum
13. Breast carcinoma		0	3	Recurrence over left clavicle and lung metastases.	Not obtained
<i>II. Cause of Death Not the Same as the Indication for Therapeutic Interruption</i>					
14. Renal disease		1	0	Diabetic coma (uremia excluded).	Not obtained
15. Polycystic kidneys		11	6	Pneumonia due to Type II pneumococcus.	Not obtained
16. Vomiting of pregnancy		3	8	Hypernephroma	Not obtained

The only postoperative deaths in the series (Cases 7 and 8) occurred in patients with cardiac disease, one of whom died of heart failure, while the other died of bilateral embolism of the lower extremities. Of the thirteen patients who died of the disease which was the indication for the therapeutic interruption, six or almost half had renal disease.

Summary and Conclusions

1. From September, 1932, to December, 1943, there were 280 interruptions of pregnancy for therapeutic indications at the New York Lying-in Hospital. During this period, 46,861 pregnant women were cared for, thus the incidence of interruption was 0.6 per cent.

2. Toxemia and cardiac disease accounted for 58.3 per cent of the interruptions.

3. Because of newer modes of therapy, interruption of pregnancy is rarely necessary now in pyeloureteritis and in vomiting of pregnancy.

4. Forty-four or 15.7 per cent were performed in the Negro race. Renal disease accounted for 68.2 per cent of all the interruptions in the Negro race, while it was the indication for only 11.2 per cent of the interruptions in the white race.

5. The average age was 25 to 35. Eight or 2.8 per cent of the interruptions were performed in women under 20 years of age.

6. The greatest number, 124 or 44.3 per cent, were performed in the eighth to the tenth week.

7. At the time of interruption, 72 or 25.6 per cent of the patients had no living children, 75 or 26.3 per cent had one living child, while the remaining 133 or 48.1 per cent had two or more children.

8. Forty-nine or 17.8 per cent of the interruptions were performed in the first pregnancy; 35 of these women never became pregnant again, three had a second therapeutic interruption, while 11 had subsequent pregnancies.

9. Pregnancy had been previously interdicted in 100 or 35.7 per cent. Subsequent pregnancy occurred three times after previous sterilization, two of which had been done elsewhere.

10. Two hundred and four, or 72.8 per cent of these pregnancies were terminated by the vaginal route, while a laparotomy was performed in 76 or 27.2 per cent.

11. Tubal sterilization was performed in 98 or 35 per cent, while 113 or 40.3 per cent were given contraceptive advice.

12. Thirteen or 6.4 per cent of the interruptions which were performed by the vaginal route were incomplete, and rupture of the uterus occurred in three cases or 1.5 per cent.

13. One hundred and fifty-seven or 56 per cent of these operations were performed under inhalation anesthesia, 102 or 36.4 per cent were performed under basal and local anesthetics, while 21 or 7.6 per cent received avertin anesthesia.

14. Two or more days of fever occurred in 60 or 21.6 per cent, while 163 or 58.2 per cent were afebrile.

15. Thirty-eight pregnancies occurred in 30 women after a previous pregnancy had been interrupted for therapeutic reasons; eleven of

these were terminated for the second time, while two spontaneous abortions and 25 deliveries occurred.

16. Eleven or 3.9 per cent of the patients who had had a therapeutic termination at the New York Hospital required an interruption in a subsequent pregnancy. When we include those who had their first therapeutic interruption elsewhere, 29 repeat terminations of pregnancies were done in 26 patients, the incidence thus being 10 per cent.

17. There were sixteen deaths; two of these occurred in the post-operative period. Thirteen were due to the disease which was the indication for the therapeutic interruption, while three were due to other causes.

PREGNANCY IN A RUDIMENTARY HORN OF THE UTERUS

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PREGNANCY of a rudimentary horn of the uterus is rare. A review of the literature indicates that case reports are less frequent in recent years. The serious nature and rarity of this condition, and the circumstance under which the present case was found, appear sufficient reasons for the case report and brief review of the literature.

Williams Obstetrics¹ makes the following statements concerning this: "In 78 per cent of 84 cases collected from the literature by Keherer in 1900, the proximal end of the rudimentary horn did not communicate with the uterine cavity, so that in them pregnancy must have followed external migration of the spermatozoa or of the fertilized ovum. Rupture often occurs in the first 4 months and may lead to death from intraperitoneal hemorrhage. This result was noted in 87, 47.6 and 5.5 per cent of the cases collected by Sanger, Keherer, and Beckmann, respectively, in 1884, 1900 and 1911." In *Principles and Practice of Obstetrics*, DeLee² makes the following comment: "Mauriceau and Vassal in 1669 recorded the first case, and now over 100 have been described." Curtis³ in his textbook says: "Bicornate uterus with one or the other rudimentary and partially hollow is said to be a common form." Davis⁴ says that "pregnancy in a rudimentary horn is an exceedingly rare condition."

After reading these statements, one is impressed with the fact that a recent review of this condition has not appeared, and only a few case reports are noted in American literature. It seems that the mortality in the early case reports was high, and they were, therefore, reported. In recent years, improved surgical measures have reduced the mortality and apparently the number of case reports. The diagnosis is usually made at the time of operation or at autopsy, as occurred in the present case report.

With the aid of the librarian of the Iowa State Medical Library at Des Moines, I have been able to review the records of 9 case reports, which have been reported since Beckmann's review in 1911. The present review is given in tabular form, and includes only a few remarks concerning the most interesting points in each. There were no deaths among these 9 case reports, but there were many complications and a few near deaths. There was a microscopic lumen between the rudimentary horn and the cavity of the uterus in only two of these. (Table I.)

TABLE I. REPORTS OF PREGNANCY IN RUDIMENTARY HORN OF THE UTERUS

AUTHOR	AGE AND SITE	REMARKS
Scott, E., and Forman, J.: AM. J. OBST. 73: 470, 1916.	45, Right side Full-term twins.	Cramps for 2 weeks at term. No more cramps or life felt. Had 2 babies before this, two shortly afterward, then 3 miscarriages, and 9 years later a baby. At operation for mass present 20 years found bones of twins in the rudimentary horn.
Lahman, A. H., Kilkenney, G. S., and Mietus, A. C.: AM. J. OBST. & GYNEC. 42: 534, 1941.	26, Right side. Full-term twins. Small canal with uterus.	Uterus small at term. Friedman positive and waited 6 weeks. No more fetal motions. Negative Friedman, positive x-ray. At operation macerated twin females in rudimentary horn.
Humpstone, C. P.: Surg., Gynec. & Obst. 31: 505, 1920.	30, Left side. Ruptured at 4 months.	Sudden severe pain. At operation for ectopic pregnancy, ruptured pregnant rudimentary horn of uterus found.
Ibid.: Case II.	21, Right side. 8th month.	Eclampsia at 8 months. Attempted vaginal section failed and removal of uterus with rudimentary horn made a difficult operation.
D'Arcy, C. E.: M. J. Australia 2: 373, 1925.	35, Left side. Full term.	Few pains and bleeding at term. Became ill 3 weeks later with fever and vomiting. Large left pregnant and small right rudimentary horn found at operation.
Stabler, F.: Newcastle M. J. 2: 117, 1931.	Age not given. Left side. 8th month.	Two previous premature births. Pains began at 8th month. Medical induction of labor failed. Normal pregnancy 2 years later, and could not deliver previous fetus. Operation 2 months later found pregnant rudimentary horn.
Nokes, J. M.: AM. J. OBST. & GYNEC. 28: 250, 1934.	19, Left side. 6 months.	Abortionist tried to interrupt pregnancy at 5 months and again at 6 months but failed, fetus killed. At operation 2 months later, found true condition.
Rutherford, R., and Morgan, J.: Lancet 2: 1337, 1934	35, Right side. Full term.	False labor at term with death of fetus. Induction of labor failed, sepsis developed and patient survived difficult operation on rudimentary horn pregnancy.
Guerrant, E.: S. Clin. North America 15: 537, 1935.	33, Right side. 5th month. Small lumen to uterus.	Normal pregnancy to 5th month, when slight bleeding occurred. Friedman test negative. Author thinks she is lucky to be alive after so long delayed operation.
Present case	31, Left side. 5th month.	Sudden death at 4½ months.

Case Report

Mrs. L. G., aged 31, married 5 years, had been pregnant about 4½ months, and had been seen last by her physician about 6 weeks previously. The county attorney of a neighboring county about 60 miles distant called me one evening and asked if I would come there and make the necessary postmortem examinations in a death that had occurred there under suspicious circumstances. On account of the medicolegal aspects of the case and gas rationing, this request was refused. Later that night he called again and agreed to bring the body to Cedar Rapids. As county coroner's pathologist of my own county, I felt somewhat obligated to help clear up the cause of death in this case, and arranged to make the necessary examinations the next day.

The woman living in a "trailer house," had enjoyed good health during her pregnancy and had last seen her physician 6 weeks previously at 3 months. On this particular morning, she did not feel well and asked her husband to stop the radio program, while he went out to do some morning chores. When he returned 15 minutes later, he found

her dead in bed. He called in a neighbor, who called a funeral director. He asked who her physician was and found that she had not seen a physician during the last six weeks. The county coroner and county attorney were not satisfied with this story and ordered an inquest and an autopsy.

The necropsy revealed that her death was due to intraperitoneal hemorrhage. There was slightly more than 2 liters of blood clots and bloody fluid in the abdominal cavity. A male fetus 19 cm. long and weighing 178 grams was found in its sac, and the placenta was attached to what was at first thought to be a ruptured Fallopian tube, but which upon further investigation, proved to be a rudimentary horn of the uterus.



Fig. 1.—Uterus with left rudimentary horn ruptured, and ovary and tube attached. Right ovary and Fallopian tube in normal position.

Autopsy Report.—The uterus is 12 cm. long. The rudimentary horn is ruptured and the fetus and part of the placenta have escaped into the abdominal cavity. The rudimentary horn is 12 cm. long by about 8 cm. across. It is attached to the lower left side of the uterus by a pedicle about 15 mm. across. Microscopic sections of this base of the rudimentary horn failed to reveal any lumen connecting the cavity of the rudimentary horn with the cavity of the uterus. The right tube and ovary are in the normal position. The left ovary is 6 by 4 cm. by 1 to 2 cm. thick. It contains a corpus luteum 15 mm. across. The left Fallopian tube is 10 cm. long by 4 to 7 mm. across. It opens into the base of the rudimentary horn. The relations between the rudimentary horn and the uterus and ovaries are shown in Fig. 1.

Comment

Any one obstetrician probably will see not more than one case of this kind and many have not seen one in many years of practice. A rudimentary horn of the uterus may be found more often by surgeons and gynecologists, who by its timely removal, may prevent sudden death later or difficult obstetric conditions.

It has been estimated from textbooks that 90 per cent of rudimentary horn pregnancies rupture about the fourth month, and may result in sudden death from intraperitoneal hemorrhage. The remaining 10

per cent may go to term and cause considerable trouble and result in the death of the fetus. In the present review, four of nine cases reported went to term. The cases reported in recent years have been the cause of considerable surgical and diagnostic difficulties, and the authors have reported them for the benefit of others. One was left in place for 20 years, and another for 2 years, before the diagnosis was made. An abortionist failed in two attempts to deliver the fetus. Twins occurred in two instances.

Summary

The sudden death of a woman in the fifth month of pregnancy, due to the rupture of a pregnant rudimentary horn of the uterus, is reported. This report with a brief review of recent American and English literature is given to call attention of gynecologists and obstetricians to the dangers and complications of this condition.

References

1. Stander, H. J.: Williams Obstetrics, New York, 1941, D. Appleton-Century Co., p. 709.
2. DeLee, J. B., and Greenhill, J. P.: Principles and Practice of Obstetrics, Philadelphia, 1943, W. B. Saunders Co., p. 532.
- ✓ 3. Curtis, A. H.: Obstetrics and Gynecology, Philadelphia, 1934, W. B. Saunders Co., Vol. III, p. 664.
- ✓ 4. Davis, C. H.: Gynecology and Obstetrics, Hagerstown, Md., 1935, W. E. Prior Co., Vol. I, Chapt. 14, p. 5.

POSTOPERATIVE VESICO-UTERINE FISTULA

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MRS. M. B., aged 47 years, was referred to me for vesicovaginal fistula with total leakage of urine.

The history was that in October, 1943, a curettage, high amputation of the cervix, and anterior and posterior colporrhaphy had been performed for rectocystocele and first degree prolapse. The day following operation it was noted that all urine escaped from the vagina.

I saw the patient five months after the original plastic operation had been performed. The repair of the prolapse was excellent. The introitus was small, good perineum, no cystocele, the uterus high, ante-flexed, cervix amputation flush with the vault. A steady stream of urine oozed from the external os.

A metal catheter through the urethra showed the bladder empty and contracted. A probe passed through the external os eventually was maneuvered through the fistula, 2 inches above the vaginal vault (cervix amputated), and then came into direct contact with the catheter in the bladder.

I considered it unjustified to plug and shut off the vagina with a rubber bag and then to distend the bladder in order to visualize the site of the fistula through a cystoscope. This procedure might have forced fluid through the Fallopian tubes into the peritoneal cavity.

At operation, one week later, it was found that the uterus would not budge or descend on volsellar traction. The cervix was fixed fairly close to the symphysis pubis. A deep Schuchardt incision extending to the cervix was made on the left side. An inverted T-incision through the mucosa of the short anterior vaginal wall, hugging the anterior wall of the uterus closely, was made. By sharp dissection the separation was

tunneled upward, the tissues proving semicartilagenous in consistency. A transverse tear into the bladder was made, by accident, immediately behind and below the internal urethral meatus. Painfully and slowly the dissection was carried upward, never obtaining a tunnel more than $1\frac{1}{2}$ inches wide until, at 2 inches above the cervix, as the probe had shown, bladder and corpus were fused in the midline. This area was almost inaccessible. With a scalpel a thin ovoid area was cut out of the anterior wall of the uterus. The fistula was situated in the center of this uterine patch. With great difficulty two sutures of No. 0 chromic catgut were passed through the bladder muscle and fascia as well as through the patch, thus adequately inverting the bladder defect. The uterine end of the fistula was disregarded. Next, the transverse hole in the bladder, which had been made during my approach, was closed with interrupted catgut sutures, and the vaginal mucosa approximated without drainage. A permanent mushroom catheter was inserted into the bladder. Finally, the Schuchardt incision was closed. The patient made an uneventful recovery, was discharged on the sixteenth day with full continence and control.

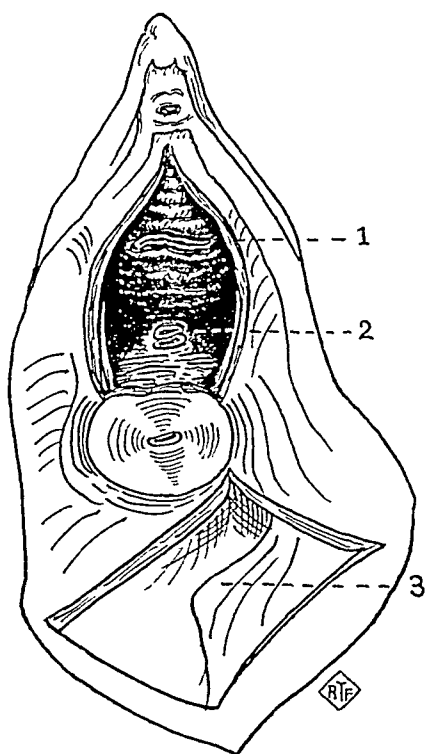


Fig. 1.

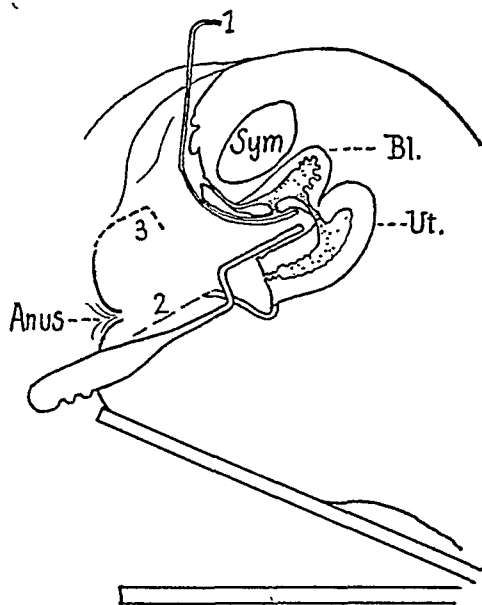


Fig. 2.

Fig. 1.—Operative exposure of fistula. Bladder and uterus separated. 1, Tear into bladder resulting during liberation. 2, Vesical and uterine openings of fistula after cutting across fistulous tract. 3, Schuchardt incision.

Fig. 2.—Diagrammatic sagittal section of pelvis. The vesicovaginal septum has been entered by means of sharp dissection up to the fistulous tract. 1, Ribbon retractor anteriorly. 2, Schuchardt incision. 3, High perineal body before operation which was restored as a final step in the procedure.

Comment.—The possibility of injuring the bladder arises whenever this viscus is separated from the uterus, either from below or above. The danger is minimized by keeping close to the uterus and finding the loose layer of areolar tissue which binds uterus and bladder to each other. If the bladder has been injured, it must be repaired at once and kept at rest and contracted by means of a permanent catheter for from eight to ten days. Less avoidable is necrosis, due to ischemia following radical hysterectomy in which branches of the vesical arteries have been tied. Drainage gauze must not touch the bladder; rubber dam, on the other hand, rarely if ever, causes necrosis. This case is reported because of the unusual technical difficulties resulting from antecedent plastic repair.

CARCINOMA FOLLOWING PREGNANCY WITH SPONTANEOUS CURE

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DIFFUSE carcinoma of the peritoneum and mesentery is generally metastatic. It is usually inoperable because of its extensive spread and involvement of adjacent organs. Occasionally deep x-ray therapy yields palliative relief, but actual elimination of the lesion and complete recovery are rare. Ewing states that there has been no case of spontaneous cure of carcinoma reported in medical literature. An instance in which intraperitoneal carcinoma was found at operation, and found absent on later laparotomy and biopsy, is of unusual interest.

G. M., a 34-year-old primipara was delivered spontaneously after a short labor, on Nov. 22, 1939. Her pregnancy had been normal in every respect. Her previous medical history was negative except for an appendectomy in 1932. Her immediate postpartum course was uneventful, and she was discharged from the hospital on the tenth day.

Soon after her discharge from the hospital she began to complain of colicky pains in the upper abdomen, weakness, fatigue, epigastric fullness, nausea and vomiting, anorexia, frequency of urination, and loss of weight. These symptoms became gradually worse, and on repeated examinations the only physical finding was a small, tender pedunculated fibroid attached posteriorly to the uterus. She was advised to remain under observation because of the above symptoms and findings. She was seen again three and a half months later, still complaining of the above symptoms. In addition to the pelvic findings described above, there was a large, tender, fixed mass in the midabdomen, not connected with the pelvic tumor. The liver was also enlarged and tender.

X-ray study of the gastrointestinal tract at that time revealed no evidence of gastric or duodenal ulcer or a new growth. A mass density in the right upper quadrant, which was extracolonic and extrarenal, was suggested.

She was admitted to the hospital four months post partum, and upon laparotomy it was found that there was free hemorrhagic fluid in the peritoneal cavity. The liver was enlarged and nodular and the seat of numerous metastatic nodules. There were multiple implants on the peritoneum and in the omentum. There was also a large, firm mass involving the gastrocolic omentum and the transverse colon. It was not possible to say whether this mass arose from the lumen of the gut. The uterus was the seat of two pedunculated fibroids, and both ovaries were studded with peritoneal implants. Several implants were taken for biopsy. An attempt was made to take a liver biopsy, but was abandoned because of extensive friability and marked bleeding.

Microscopic sections revealed lymph nodal tissue replaced by masses of atypical and hypertrophied tall cuboidal or polygonal epithelial cells which in places form suggestions of glands, and occasionally contained small mucuslike globules. These cells had large hyperchromatic vesicular nuclei and mitotic figures of both regular and irregular types. Pathologic diagnosis was metastatic adenocarcinoma.

The immediate postoperative course was very stormy. She was markedly distended and vomited; the temperature was persistently ele-

vated, the pulse poor, and outlook grave. After several days the distention diminished, the temperature declined, food was tolerated, and she appeared much better. The abdominal wound healed by primary union and she was discharged on the fourteenth postoperative day.

When seen two weeks later she complained of headaches, weakness, vomiting, and exhaustion. The abdomen was distended, tender, and presented evidence of free fluid in the peritoneal cavity. The liver was



Fig. 1.—Low-power section of fibrosed omentum containing a highly cellular tumor whose cells are arranged in cords suggestive of incomplete gland formation. Specimen was removed at first operation.

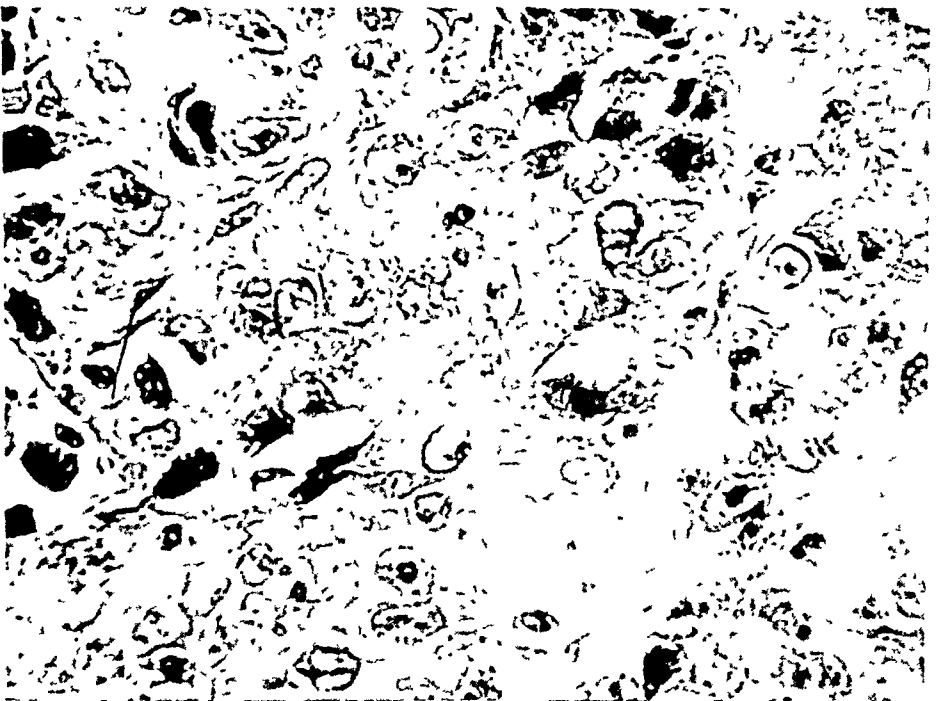


Fig. 2.—High-power section of Fig. 1, composed of polygonal epithelial cells with hyperchromatic nuclei and mitotic figures. Multinucleated tumor cells are also present.

palpable, and multiple masses were still felt in the abdomen. A few weeks later the spasticity and tenderness in the upper abdomen still persisted but the masses were not felt, and the liver enlargement receded. She still complained of some pain in the upper abdomen, but vomiting had ceased, her appetite had improved, and she had gained 4 pounds.

Six weeks later she stated she had menstruated for the first time since her delivery. She felt nervous, had slight abdominal pain, and had gained eleven pounds. There was still slight tenderness in the upper abdomen, but no masses were palpable. The liver could not be felt. For the next year she remained under observation and continually showed improvement. Her weight, although remaining stationary, was normal; her menses were regular, and she had no complaints.

In April, 1943, three years postoperative, she was found to be pregnant, but because of her previous history and findings, she was admitted to the hospital for study and consultation. The surgical, medical, and pathological departments were consulted. In view of the previous history and operative findings, they all advised termination of the pregnancy by abdominal hysterotomy and sterilization.

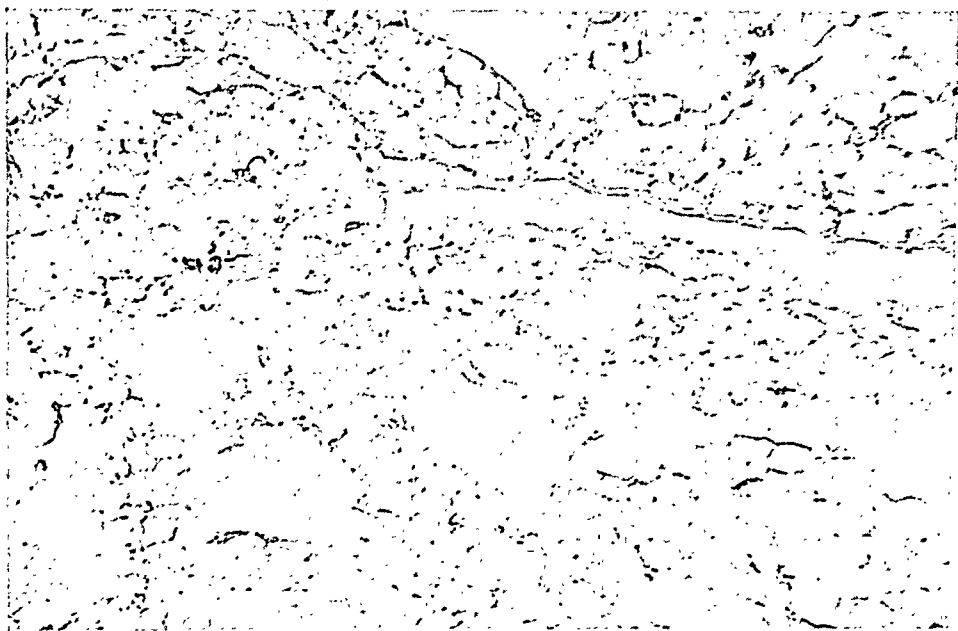


Fig. 3.—Section of omentum removed at the second operation showing normal fat tissue and no malignancy.

At operation the liver edge was found to be regular and smooth. There were a few soft adhesions between the omentum and the parietal peritoneum. There were no implants on the peritoneum, omentum, or other abdominal viscera. The uterus was enlarged, bluish, soft, with several pedunculated fibroids on its posterior wall and a larger degenerated fibroid on the left side. There were, in addition, numerous subperitoneal elevations on the fundus of the uterus and suggestions of peritoneal implants. Both ovaries and tubes were normal. Because of these subperitoneal elevations, a total hysterectomy with bilateral salpingo-oophorectomy was performed. Small pieces of omentum were removed for study. Microscopic study of the uterus, tubes, ovaries, and sections of omentum revealed no evidence of carcinomatous degeneration. The postoperative course was smooth and uneventful. The patient was discharged on the fourteenth postoperative day.

She has since been seen on several occasions and except for slight menopausal symptoms has no other complaints. At the present time there is no evidence of recurrence of the neoplastic lesion found four and a half years ago at the first operation.



A.



B.

Fig. 4.—A, Hemisection of left ovary removed at second operation with corpus luteum verum. B, Hemisection of right ovary removed at second operation showing a normal functioning ovary with multiple follicular cysts. In neither ovary was any malignancy present.

Discussion

There is abundant experimental evidence in animals suggesting that persistent estrogen therapy produces atypical cancerous and precancerous lesions of the accessory genitalia. There are also reports of the production of cancer of the breast in the human female by indiscriminate use of massive doses of estrogenic substances. The prevalence of genital and breast cancer in women past the menopause is explained by Allen as due to the continuous abnormal stimulation of estrogen, unopposed by progesterone, which ceases to be secreted at the climacteric.

Some investigators maintain that pregnancy causes cancer of the cervix to grow very fast and invade the lymphatics, but others, such as Frank, and Peller and Emge hold an opposite view. Mankin claims that pregnancy retards existing carcinoma of the cervix and breast. DeLee and Greenhill state, on the other hand, that the termination of pregnancy by birth or abortion significantly increases neoplastic growth

and that during pregnancy progesterone checks the carcinogenic action of estrin. They also maintain that after the end of pregnancy, estrogen acts unopposed to promote the growth of the lesion because the titer of progesterone is markedly diminished. This explains the extensive growth of the lesion in this case soon after delivery, but it throws no light on its subsequent spontaneous disappearance as demonstrated by later laparotomy and clinical observation.

References

- Allaben, G. R., and Owen, S. E.: J. A. M. A. 112: 1933, 1939.
 Allen, E. S.: Kentucky M. J. 25: 615, 1927.
 Auchincloss, H., and Haagensohn, C. D.: J. A. M. A. 114: 1517, 1940.
 DeLee, J. B., and Greenhill, J. P.: The Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Co., p. 550.
 Emge, L. A.: AM. J. OBST. & GYNEC. 28: 682, 1934.
 Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, 1940, W. B. Saunders Co., p. 46.
 Frank, L. W.: Kentucky M. J. 40: 165, 1942.
 Hoffman, J.: Female Endocrinology, Philadelphia, 1944, W. B. Saunders Co., pp. 38-41.
 Mankin, Z. W.: Arch. f. klin. Chir. 199: 337, 1940.
 Mundell, J. J.: AM. J. OBST. & GYNEC. 13: 86, 1927.
 Parsons, W. H., and McCall, E. F.: Surgery 9: 780, 1941.
 Peller, S.: Die Geburtstod, Vienna, 1936, Franz Deuticke.

960 STERLING PLACE

877 EMPIRE BOULEVARD

PREGNANCY AFTER RENAL BIOPSY IN HYPERTENSIVE DISEASE

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ALTHOUGH the final kidney changes associated with death from hypertensive disease and its complications are rather well established, knowledge of the intervening steps has been largely lacking. Recently, however, studies¹⁻³ of renal biopsy material have given a better understanding of the actual kidney picture in the various grades or stages of hypertension. As one example of the importance of these observations, it has now been reported that in at least some cases the vascular changes are primary outside of the kidneys, thus indicating that true essential hypertension without renal changes does exist. Also, even when the kidney vessels themselves are involved, it has been shown that there may be at first no demonstrable renal parenchymal or functional alterations. Moreover, there is some reason to believe that the procedure for obtaining renal biopsy material, being reasonably safe, may offer valuable additional information as a guide in surgical treatment of hypertension.

It was in such a patient who had been investigated for possible surgery that pregnancy occurred, thus presenting the first instance, so far as I have been able to determine, of pregnancy complicating hypertensive disease with renal biopsy findings. The case report is of some interest for its uniqueness. There is also the suggestion here that data accumulated from this and other cases could conceivably in time establish histological standards for prognosis and treatment in hypertensive women who become pregnant. These women make up a large group of obstetric patients, for many of whom all the tests devised up to the present time have offered little more than the vaguest information regarding the outcome to be expected.

Case Report

Harper Hospital, No. 241491. The patient was 30 years old and had been married five years, with no pregnancies. She was admitted to the hospital March 16, 1942, with the history of headaches beginning eight years before and gradually becoming frequent and very severe. High blood pressure had been discovered several weeks before admission when a physician was consulted for sudden, sharp pain in the left side of the chest. The past history was negative for infections or other causes of hypertension. The patient's father had lived to be 86 years of age. Her mother died of dropsy and heart trouble at 56 years of age. Several brothers and sisters were well, but one brother, 44 years old, was said to have high blood pressure.

On admission the blood pressure was 205/120. The heart was slightly enlarged, but sounds were clear and of good tone. Fundusoscopic examination showed no neuroretinitis. Some of the retinal arteries were tortuous and smaller than usual but not definitely constricted. The veins were rather full, but there was no arteriovenous nicking. Otherwise the physical findings were unimportant.

All the usual laboratory tests as well as many special studies were made, with results of the more important ones as follows: The Kahn test was negative for syphilis, and a chest x-ray showed only slight cardiac enlargement. Urinalyses were all negative for albumin and glucose, and specific gravity varied between 1.018 and 1.030. A complete blood count gave normal findings. Fasting sugar was 0.115 Gm., nonprotein nitrogen 40.2, and later, 33.8 mg., and chlorides as NaCl, 495 mg. per 100 c.c. of whole blood. The total serum proteins were 6.16 Gm., the albumin being 4.41 and globulin 1.75, thus giving an albumin-globulin ratio of 2.5 to 1. Blood urea clearances (110 and 119 per cent) indicated normal function. In a cold pressor test with immersion for ten minutes, the maximum elevation of blood pressure occurred in two minutes from an initial 204/128 up to 224/128. Fourteen minutes after immersion the two readings were 200/130. Nitroglycerin, $\frac{1}{100}$ grain, under the tongue caused a maximum drop of blood pressure in five minutes to 188/132 from 206/130. Cystoscopic examination, with ureteral catheterization, was entirely negative except for slight constriction of the left ureter, and a retrograde pyelogram showed no x-ray evidence of urinary tract abnormality.

On March 16, 1942, through an incision in Petit's triangle the lower pole of the right kidney was exposed by Dr. F. C. Cole, and a biopsy specimen obtained with the special punch designed by Dr. T. N. Horan. Various stains of sections from this tissue showed arteriosclerosis of all arteries and arterioles. There were, however, no necrotic areas and no demonstrably definite glomerular or tubular changes although there was some question regarding the tubular epithelium in certain areas. According to the descriptions of Castleman and Smithwick, the picture was that of moderately advanced renal vascular disease and was comparable to their Grade 2 (Figs. 1 and 2).

After discharge from the hospital there was only one menstrual period, which began April 24, 1942, and on August 11 the uterus was found to be enlarged to the size of fourteen to sixteen weeks' pregnancy. At that time the only finding of importance was a blood pressure of 220/135. In view of the dangers anticipated, interruption of pregnancy was advised, but this was refused.

The pregnancy progressed uneventfully, except for persistence of the hypertension and headaches, until about the beginning of the thirtieth week. Total weight gained was 14 pounds. On Nov. 14, 1942, albuminuria was noted for the first time. This increased from slight to marked degree, and many hyaline casts had appeared by November 18, although the systolic blood pressure remained around 220. After admission to the hospital on November 20, the ordinary and special tests were repeated with essentially normal results in most instances. Whole



Figs. 1 and 2.—Sections from renal biopsy material, magnified 100 times. Marked arteriosclerosis of small arteries and arterioles. No demonstrable changes in glomeruli or tubules.

blood nonprotein nitrogen varied between 26.5 and 33.8 mg. per 100 c.c. and was 28 mg. on the day of delivery. The plasma CO₂ volume per cent was 52 and the blood cholesterol 277 mg. per 100 c.c. Total serum proteins were 5.0 Gm.; the albumin being 3.3, and globulin 1.7, thus giving an albumin-globulin ratio of 1.9 to 1. Urea clearance was well within normal limits. One appreciable deviation from normal was found in the phenolsulfonphthalein test in which the first 15-minute elimination was reduced to 15 per cent. Also, the eyegrounds now showed definite nicking of the veins, but no neuroretinitis.

The course in the hospital was marked by an initial slight lowering of blood pressure to 205 systolic, but with return after a few days to readings varying from 220 to 235. Albuminuria continued, and along with this occurred hyaline and granular casts in increasing numbers. Headaches now became progressively worse until by the end of a week the patient complained of almost constant pain in the head which was so intense as to greatly interfere with sleep. Vomiting also became frequent. In view of these distressing and alarming symptoms delivery seemed urgent, and in the interests of the premature child, cesarean section was decided upon.

On Nov. 28, 1942, classical cesarean section was done under general anesthesia. Sterilization had been suggested but was refused. The child, a 4 pound 1 ounce male, was in good condition at birth but died of prematurity and atelectasis after forty-nine hours. Recovery of the mother from the surgical standpoint was uneventful. The placenta showed no infarcts of appreciable size or any other abnormality. It is noteworthy that at the time of operation the kidneys seemed to be of normal size and shape, and there was no palpable evidence of suprarenal tumor.

After an immediate postoperative drop in blood pressure, the former levels of 220 to 235 systolic soon returned and were maintained during the stay in the hospital. Albuminuria gradually diminished until only a trace of albumin was present. An outstanding change was the complete relief from headaches within forty-eight hours. On the fourth day post partum the left retina was found to have a definite exudate below the macula, as well as more marked nicking of the veins and occlusion of a few of the vessels. Examination during the next 23 months showed somewhat higher blood pressure levels (250/155 on Oct. 30, 1944) with slight albuminuria and occasional hyaline casts persisting.

This case tends to confirm the previously debatable but yet commonly held clinical opinion that essential hypertension (without kidney changes except for arteriosclerosis) is likely to go on to renal functional impairment when complicated by pregnancy. It also adds some weight to the belief that, in addition to the immediate dangers, these patients are usually left worse off by the pregnancy; even though, as in this instance, emptying of the uterus is instituted with the early signs of renal parenchymal involvement. Much less definite, but in accord with our experience, is the suggestion here that these patients will do well with operative intervention, provided it is undertaken before the onset or early in the development of renal insufficiency.

Grateful acknowledgment is made for the valuable advice and assistance of Dr. H. A. Freund, Dr. A. H. Price, and Dr. W. B. Cooksey of the Department of Medicine, Harper Hospital.

References

1. Freund, H. A., Cole, F. C., Horan, T. N., and Miller, S.: Harper Hosp. Bull. 1: 129, 1942.
2. Castleman, B., and Smithwick, R. H.: J. A. M. A. 121: 1256, 1943.
3. Talbott, J. H., Castleman, B., Smithwick, R. H., Melville, R. S., and Pecora, L. J.: J. Clin. Investigation 22: 387, 1943.

A DEMONSTRATION MODEL FOR UTEROTUBAL INSUFFLATION*

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IN RESPONSE to the need of demonstrating to medical students and physicians the method of uterotubal insufflation, the present working model has been developed. It has undergone several stages of improvement. In its present form it consists of three major parts constructed out of three plastic media:

1. A translucent posterior section, cast in cellulose acetate, $\frac{1}{32}$ inch thick, represents the abdominal viscera in natural size and is painted approximately in their natural colors.

2. An anterior section formed of plexiglas represents the peritoneal cavity, and consists of a double-walled water container or jacket $\frac{1}{8}$ inch thick which is clear and transparent. Its shape is modeled after the contour of the abdominal wall and the underlying viscera. A narrow space occupying its major portion is expanded somewhat above where it is closed by a transverse bar at the level of the natural diaphragm. It is provided with a spout through which water or mineral oil can be introduced to act as the medium through which CO_2 is percolated. The lowermost portion of the water jacket is expanded to contain the uterus, tubes, and ovaries, and conforms to the configuration of the female pelvis. At the pelvic brim the intestines have been artificially modified so as not to obscure the genital organs which are transilluminated by means of an electric light placed behind the supporting display panel. The lower pole of the expanded plexiglas chamber is perforated at an angle to allow the cervix to project into the vaginal canal.

3. The external genitalia (vulva) are carved out of solid lucite hollowed out at its center to represent the vagina, which permits the introduction of a small-sized speculum. The uterus and adnexae are cast in cellulose acetate; the cervix is held in place by two plexiglas colarettres on the inside and outside and cemented by a waterproof compound.

NOTE.—The year 1945 marks the twenty-fifth anniversary of the employment of tubal insufflation for diagnostic purposes. The first trial was made in the x-ray department of the Mt. Sinai Hospital. In this woman the abdominal wall was seen by those present to rise and the conclusion was reached that the gas (oxygen) must have entered the peritoneal cavity via the uterus and through the Fallopian tubes, producing a subphrenic pneumoperitoneum in that patient as demonstrated later by the x-ray films. The use of oxygen gas was found safe and harmless but, later, carbon dioxide was substituted as being even safer and more rapidly absorbed. This first patient upon whom the method was tried became pregnant within two months and further experiments were made to determine the tolerance, the amount of gas necessary, the pressure under which it was introduced, the possibility of infection, the danger of embolism, the interpretation of the findings and their reliability in diagnosis, as well as the indications and contraindications.

The first full report was made in 1920 and was based on 55 cases. Other observers supplemented this by accounts of their own experiences, and Dawson Furniss, in his paper published in 1921, applied to the procedure the name of its originator, and it is now widely known as the Rubin test. Modifications and improvements, with combinations of kymograph tracings and other features have marked the progress in this field of an outstanding contribution to American gynecologic practice.

The Editor.

*Made by The Displayers, New York, N. Y.

A metal uterine cannula is firmly cemented into the cervical canal which communicates with a hollowed-out uterine cavity. Two metal tubes are channeled through the Fallopian tubes as far as the fimbriated ends in order to allow the CO_2 to pass into the water chamber. The outer end of the cannula is fitted with a stopcock to prevent the water or mineral oil from leaking.

The model as it stands is light, portable, and durable, having the advantages of plastics, which are superior to plaster models or those made out of papier-mâché or glass. It withstands rough usage better than plaster anatomy models, which, besides being heavy, are extremely fragile. A compact folding arrangement on the back of the display panel makes for easy setup and supports the model at exactly the correct angle. Here also a small hinged door provides easy access and free ventilation for the light which illuminates the viscera. By means of a chromium reflector the light is especially concentrated upon the uterus and tubes.



Fig. 1.—Diagrammatic representation of model.

The illumination from behind the genitalia is re-enforced by a light shining from above. Their combined effect brings out the colors of the abdominal viscera and highlights the gas bubbles as they rise toward the diaphragm in the transparent anterior water container. The effect thus produced resembles satisfactorily what actually takes place during clinical uterotubal insufflation.

To operate the demonstration model it is necessary to set the clinical insufflation apparatus at a higher level than the uterine cannula in order to prevent regurgitation into the inflow tubing. The reduction valve of the insufflation apparatus is set at 15 pounds' pressure. The

speed-regulating valve is gauged to deliver 60 c.c. per minute. The inflow glass stopcock is now opened, followed by opening the metal stopcock connecting the uterine cannula, when CO_2 will be seen to pass up in bubbles from the fimbriated ends into and through the liquid filling the water container. As the model is tilted at an angle of 45 degrees or more, the gas bubbles are seen to rise toward the diaphragm where they collect in a fashion simulating a subphrenic pneumoperitoneum. The level of the diaphragm is simulated by placing a dark cardboard which is bent over the anterior aspect of the model at the level of the mid-portion of the liver.

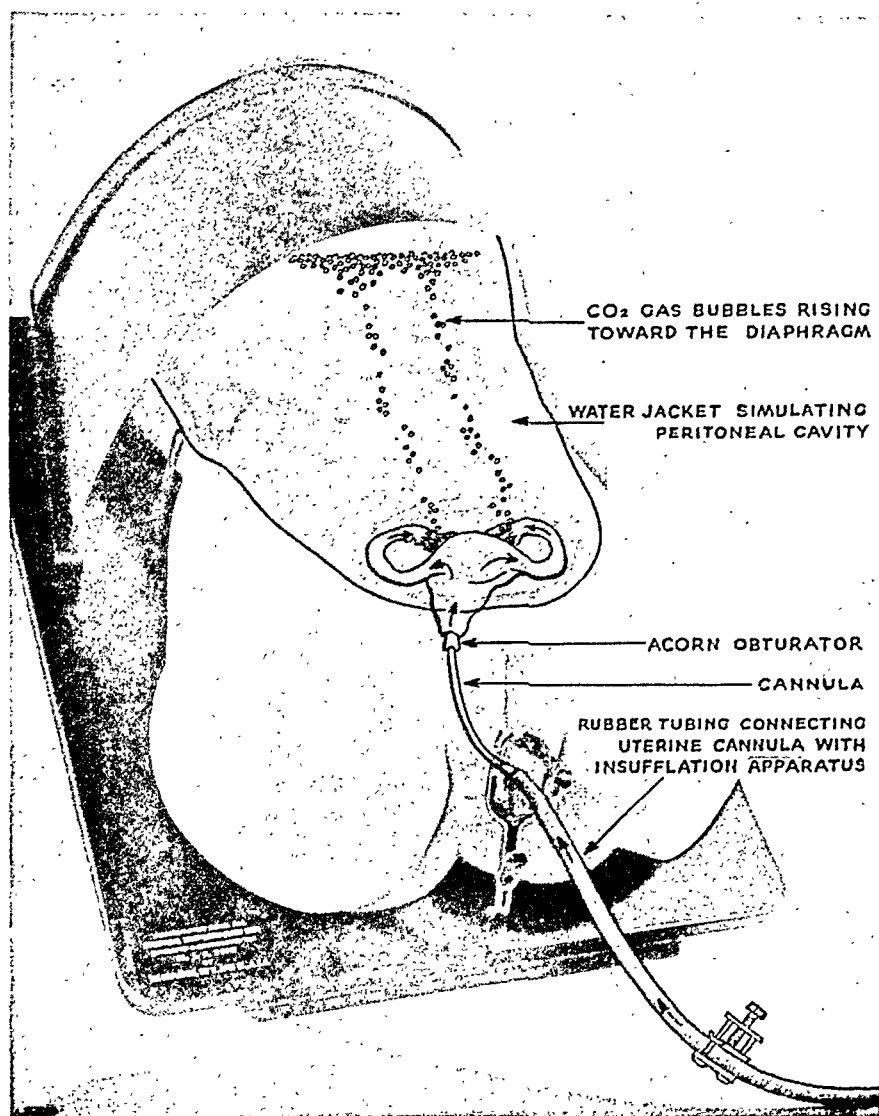


Fig. 2.—Photograph of full-sized model.

In order to reproduce the different graphs characteristic of patency, nonpatency, spasm, and partial patency of permeable strictures, a screw clamp (Murphy type) is attached to the rubber tubing near its insertion into the uterine cannula. To demonstrate tubal patency it is only necessary to allow the CO_2 gas to pass through the tube system until the bubbles appear at one or both fimbria. As the caliber of the metallic tubing within the Fallopian tubes is different, the CO_2 will be seen to escape through the wider tube. To demonstrate tubal patency on both sides it is only necessary to tighten the clamp momentarily, thus increasing the pressure which is sufficient on releasing the constriction to force the gas also through the narrower-calibered metal tubing. Both fimbria will then be seen to emit CO_2 gas bubbles. The same thing can be accomplished by momentarily increasing the speed of flow. To demon-

strate the rhythmic oscillations commonly observed in normal tubal patency and function, the clamp may be tightened and relaxed intermittently 3 or 4 times per minute. To reproduce the kymographic tracing characteristic of tubal nonpatency, the clamp should be tightened till the pressure is 200 mm. Hg. The inflow glass stopcock is closed for several seconds and then the clamp is released, thus producing a sharp drop of pressure to zero.

Spasm may be imitated by tightening the clamp till a pressure of 140 mm. Hg or higher is recorded on the kymograph, when it is relaxed till the pressure drops to 60 from 80 mm. Hg followed by intermittent tightening and relaxing the clamp, which reproduces rhythmic oscillations as met in normal tubal pregnancy.

To demonstrate the effect of tubal strictures or adhesions with partial permeability, it is necessary to tighten the clamp till the pressure rises to 150 mm. Hg or higher, and then relax the clamp slightly, allowing the pressure to drop gradually without producing oscillations.

The various effects now produced by hand can be achieved automatically by an electrical device which will eventually be available.

I wish to acknowledge my indebtedness to The Displayers, to Dr. R. L. Dickinson, Mr. Michael Brenner, and Mr. Malcolm Steiner for their valuable help in the construction of this model.

SURGICAL TREATMENT OF ABSENCE OF THE VAGINA

Report of Two Cases

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THERE should be little question as to the advisability of attempting surgical correction of absence of the vagina in suitable cases. The most common (as seen in China) and the most difficult to treat are those of traumatic origin in which closure of the vagina is secondary to the use of sharp instruments or the ill-advised instillation of strong, corrosive substances into the vagina by untrained midwives, presumably for the treatment of dysmenorrhea. Congenital anomalies of the female generative tract vary in degree from complete absence of the entire tract to minor defects. Clinically, the most common is absence of the vagina, in whole or in part, with a rudimentary cordlike uterus associated with normal ovaries, uterine tubes, and external genitalia. Frequently, this condition is not suspected until puberty, or even after marriage, as illustrated by the two cases herein described.

Developmental anomalies of the female genitourinary tract are encountered often enough so that their diagnosis and treatment demand an understanding of normal embryologic development. As the genital and urinary tracts are closely associated from the standpoint of both origin and growth, it has long been recognized that anomalies in the one may be accompanied by anomalies in the other. There is general agreement that the cervix, uterus, and Fallopian tubes develop from fusion of the

Müllerian ducts, but disagreement arises concerning the embryology of the vagina. The work of Koff¹ and the morphology of the various degrees of anomaly as seen clinically indicate that the upper two-thirds of the vagina develops from the lower portion of the fused Müllerian ducts, whereas the lower one-third originates from the urogenital sinus. There is first division of the cloaca whereby the dorsal one-third becomes the rectum. The ventral portion is further divided into three segments, the middle one of which is known as the pars pelvina. The lower portion of the vagina is formed from the sinovaginal bulbs and pars pelvina of the urogenital sinus. Meyer² has convincingly shown that the vaginal epithelium is derived from the urogenital sinus by means of invasion and replacement of Müllerian duct epithelium.

Correction of this difficulty should be attempted in young women with well-established secondary sex characteristics who are married or contemplate marriage. The difficulties encountered in the treatment of this condition have stimulated much thought, resulting in the suggestion of several operative methods. The purpose of all of these operations is to open a passage between the bladder and rectum and to provide a suitable epithelial surface. A classification into five groups according to procedure is suggested. It should be mentioned that Dupuytren in 1817 is generally considered the first to have attempted the construction of an artificial vagina.

1. *Use of the Small Intestine.*—Baldwin³ in 1904 suggested opening a space between the bladder and the rectum into the cul-de-sac. A segment of the sigmoid colon or terminal ilium is then mobilized and with its mesentery pulled downward through the pelvis and a suitable opening made and stitched to the outside skin. The middle portion of the ilium is brought downward, forming a double barrel cavity, later converted into one by a pressure clamp. The continuity of the bowel is re-established by anastomosis. However, Baldwin⁴ first performed the operation in 1907 using the lower ilium as a substitute for the absent vagina.

In 1909 Mori⁵ devised a method of using the terminal portion of the ilium but pulled down one end of the mobilized segment. Difficulty was encountered in approximating the intestine to the outside skin but the result was satisfactory.

2. *Use of the Rectum.*—The operation devised by Schubert⁶ is the best known of this group. In 1911 he described his technique, which consists of opening a space between the bladder and rectum. The rectum is dissected from the external sphincter, the coccyx removed from behind, the rectum and sigmoid colon mobilized without opening the peritoneum, and 5 inches of the rectum amputated without severing the blood supply. The amputated portion of the rectum is raised into the artificial opening and the distal end of the bowel pulled down through the sphincter and stitched to the skin. This technique may have been based on that of Sneguireff,⁷ who, in 1892, resected a portion of the rectum in constructing an artificial vagina, and on that of Popow⁸ who further developed this idea.

3. *Use of Skin Flaps.*—Several authors have suggested opening a space between the bladder and rectum and turning in skin flaps. The operation devised by Graves⁹ consists of utilizing the labia minora and skin from the adjacent inner surfaces of the thigh to cover a glass mold. The pouch is then inverted into the previously dissected opening between the bladder and rectum and secured by stitches.

An ingenious and successful tube flap operation was devised by Frank and Geist¹⁰ in 1927. A tube flap was made from the inner surface of the

thigh and the distal end gradually severed and finally inserted into a prepared space between the bladder and the rectum. The entire procedure required about three months' hospitalization.

4. *Use of Pressure.*—The most common effect of pressure is from cohabitation, which accounts for some of the shallow pouches seen in this group of women. Only a small depression is possible and is generally unsatisfactory. Falls¹¹ in 1940 described a new method. A circular disk is cut and pressed inward in the position of the proposed new cavity. Epithelization is aided by making four small flaps from the skin which are sutured to the sunken disk. Healing is usually complete in two weeks and depth is further increased by pressure with a vaginal plug. This procedure may be repeated to secure further depth.

Frank¹² in 1941 suggested a nonsurgical method of simple pressure with glass tubes of graduated sizes. He has carried out this procedure on nine patients.

5. *Use of Vaginal Mold With or Without Skin Grafts.*—Although he had described his method two years previously, Wharton,¹³ in 1940, reported a series of twelve patients operated upon by seven surgeons. His technique consists of opening a space between the bladder and the rectum into which is inserted a form of appropriate size covered by a rubber condom. The form may be of various materials but Wharton prefers balsa wood. The patient should wear the form for several weeks, or until the new canal has been thoroughly covered with epithelium. He believes that epithelization occurs from the edges of the introitus and that grafts from the skin are not necessary.

Choice of Method

In the selection of a method of treatment for this anomaly the safety of the patient must be considered more important than the final result. Undoubtedly, the Baldwin operation has been highly successful in some cases and has been enthusiastically recommended by Judin¹⁴ and by Bodenheimer and Goldman.¹⁵ Frank,¹² however, in a review of the treatment of this condition, mentions fatalities connected with this operation amounting to 17.5 per cent, which he considers to be lower than the actual. Masson¹⁶ has been an advocate of the Baldwin operation, having operated upon ten cases successfully, but more recently he has performed the operation four times with two deaths and is impressed with its danger.

In 1936, in Berlin, one of us (F. E. W.) had the privilege of seeing three patients operated upon by the Schubert technique (two by Stoeckel and one by Schubert) and although all three patients enjoyed a smooth convalescence, the danger of the procedure could not be overlooked. During the process of freeing the sigmoid colon by blunt dissection after the coccyx has been removed, there is ample opportunity to damage one of the great blood vessels. Also, the danger of infection is considerable and Frank mentions three deaths in 53 cases operated upon by the Schubert method. We believe it unjustifiable to treat a condition of no danger to the patient by a method carrying considerable risk.

The use of skin flaps turned in from the adjacent external genitalia and thighs gives an opportunity for considerable scar tissue formation. A safe procedure is the Frank-Geist operation recently described by Dannreuther,¹⁷ who successfully performed the operation and was favorably impressed with the final result but considered the prolonged hospitalization a disadvantage.

The Falls operation seems to be practical and to produce a good result but we have had as yet no experience with the method. The nonsurgical method of Frank, though time consuming, does not require hospitalization and if a canal of suitable depth can be produced by this simple method, it is to be recommended.

As previously mentioned, the most common need for surgical intervention of this kind in China is in patients with partial or complete stenosis of the vagina resulting from trauma or the action of chemicals. Many of these patients have been so mutilated with sharp hooks that the entire floor of the bladder and the anterior wall of the rectum are torn out, followed by extensive scar formation. The only possibility in such cases would be the Baldwin operation, but such extensive damage is hopeless of adequate repair. We operated upon two less mutilated patients with complete stenosis of the vagina due to trauma and elected to use a method of inserting Thiersch grafts applied to a mold of suitable size. As these two women were lost sight of, the final results cannot be reported.

A detailed report, however, of two cases of congenital absence of the vagina in which operation was performed will be given.

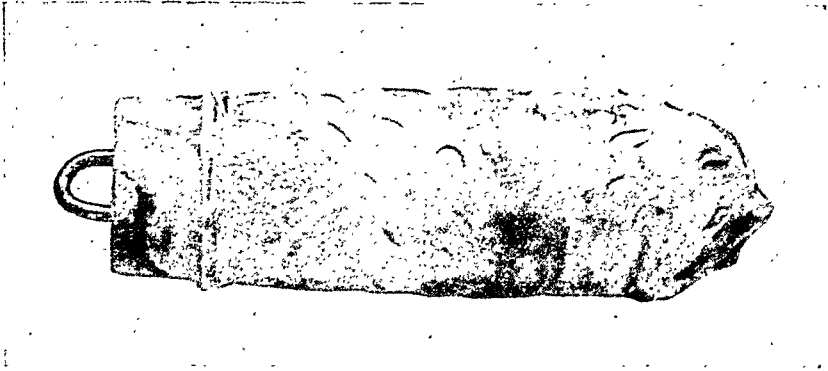


Fig. 1.—Hardwood form, which we no longer use, was covered by a rubber condom. A Thiersch graft was applied with outer surface looking inward.

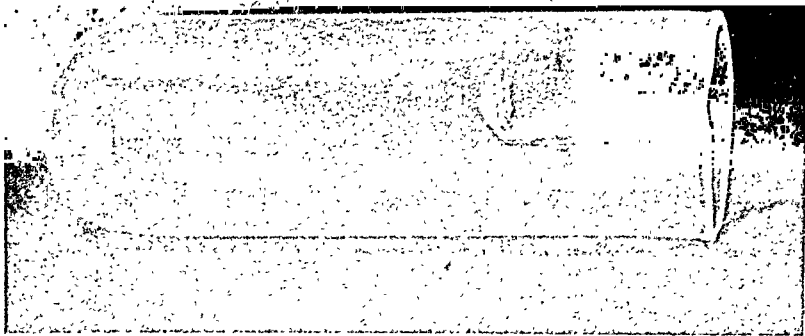


Fig. 2.—Mold of Pyrex glass which is more suitable than wood. The Thiersch graft is applied directly to the glass with the outer surface looking inward. The glass form is 11 cm. long, 3.2 cm. wide in the middle, and 3 cm. wide at each end. To protect the urethra, a groove is sunk at the open end—3 cm. by 1 cm. Glass form also permits observation of epithelization without removing form.

Technique

The patient should be prepared and draped for vaginal operation. A transverse or crucial incision should be made between the urethra and anus and blunt dissection begun superior to the rectovaginal fascia. This is easily carried up to the cul-de-sac, usually a distance of about 11 or 12 cm. Bleeding points should be controlled.

At first a wooden form (Fig. 1) covered by a condom was used. A split Thiersch graft from the inner surface of the thigh should be cut, applied with the outer surface to the mold and inserted into the prepared cavity.

Several materials have been used for the construction of this type of form. Miller¹⁸ has warned against the use of some plastic materials which may have disastrous results. Pyrex glass was selected as the most suitable material for the mold, being superior to the wooden form, but we later found that this had been suggested by Meigs.¹⁹

Counsellor²⁰ suggests using a Thiersch graft on a rubber tube and attributes the idea to Gilles and McIndoe of London, who used the principle in cranial surgery and also in the construction of the male urethra. Barrows²¹ reports a similar procedure and attributes the idea to Kirschner and Wagner, who used a rubber sponge as a vaginal mold. The Pyrex form (Fig. 2), which we have used, is 11 cm. long, 3.2 cm. in diameter in the middle, and 3 cm. in diameter at each end. At the open end it has been found desirable to sink a small groove which is 1 cm. deep and 3 cm. long. With this form inserted so that the groove protects the urethra, there is no damage to that structure from pressure necrosis even though it may be necessary to use an indwelling catheter.

After the first week, the glass form may be removed for a few minutes and the newly epithelialized cavity irrigated with normal saline or a mild antiseptic solution. By the end of two or three weeks the patients may be discharged from the hospital and treated as an outpatient.

It is just as important to keep the cavity open as it is to form it in the first place, and our previous experience with the two cases of traumatic closure of the vagina indicates that it is desirable for the patient to wear the form secured by a T-binder, a few hours a day for a period of six months. Owens²² has suggested using elastic bands attached to an abdominal belt to hold the form and graft in place and this is an improvement over the T-binder. The two patients herein described were instructed to wear the form for six months and the results were gratifying. Intercourse should do no harm two months after the operation.

Report of Cases

CASE 1.—C. S. L., a married Chinese woman 22 years of age, was seen in our gynecologic clinic on Sept. 3, 1940. She had never had any menstrual flow and experienced no periodic attacks of abdominal pain. The breasts started to develop at the age of 12 years, and pubic and axillary hair appeared when she was 15 years of age. She had been married for seven years and attempts at intercourse had been painful and unsuccessful. There was no history of trauma, infection, or the use of foreign substances in the genital tract.

The general physical examination showed essentially normal findings. The growth of hair was normal and the breasts well developed. Body contours were distinctly female in type. The external genitalia were well developed. The vagina was represented by a small pouch 4 cm. deep and 1 cm. in width. There was a small defect anterior to this dimple and some scar tissue at this point. On rectal examination, the cervix and uterus were felt together to be about 4 cm. in length. This body was narrow, cordlike, and hard, and the uterus was thought to be about the size of an olive. No other masses were felt. The blood hemoglobin was 15.3 Gm. per 100 c.c., and the urine was normal. Retrograde pyelogram and cystoscopy failed to show any congenital anomaly in the urinary tract.

The patient was operated upon, Dec. 10, 1940, by the technique already described. There was slight bleeding from the newly constructed vagina for the first three days and it was necessary to insert a stitch in the new vaginal vault corresponding in position to the base of the broad ligaments. After this, healing was uncomplicated. The glass form was removed at the end of a week and the newly formed canal was found to be covered by a thin layer of epithelium, soft and pliable, and 12 cm. in length. The patient was discharged from the hospital six weeks after operation and followed in the outpatient clinic.

Examination at the end of five and one-half months showed that the vagina was soft, there was no sign of scar tissue, and two fingers could be inserted in the introitus without difficulty. Sexual intercourse was reported to be satisfactory. The operative result in this patient is shown in Fig. 3.

CASE 2.—L. Y. F., a Chinese woman, aged 17 years, came to our gynecologic clinic on April 22, 1941, because of inability to have marital relations. She had been married for two weeks and attempts at intercourse had failed. She did not know that she was abnormal although she had never menstruated. Her medical history was irrelevant except that she had had palpitation of the heart and dyspnea on exertion for one year. On physical examination the patient was found to be somewhat underdeveloped and delicate in appearance. The breasts were small and pubic and axillary hair was scanty. The secondary sex characteristics were poorly developed and the operation was undertaken only upon the insistence of the patient and her mother in order to prevent a separation of the patient and her husband. We believe that the operation should be done only in the presence of well-developed secondary sex characteristics but felt that it was justifiable in this case and the patient was happy with the result. The heart was enlarged to the left with the physical findings of mitral valvular disease. The external genitalia were small but normal. The vagina was represented by a dimple 1 cm. in depth. On rectal examination a small lump about the size of the distal phalanx of the thumb was felt in the position of the cervix. No other masses were palpable. The blood hemoglobin was 15 Gm. per 100 c.c. and the urine was normal.



Fig. 3.

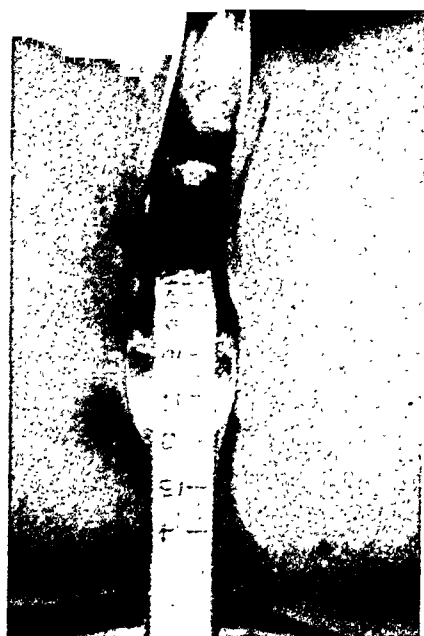


Fig. 4.

Fig. 3.—Case 1. Photograph taken nine weeks after operation. The vagina measures 11 cm.

Fig. 4.—Case 2. Photograph taken six months after operation. The vagina in this case also is 11 cm. in depth.

The patient was operated upon, May 17, 1941, according to the described technique. Her postoperative course was smooth except for difficulty in urination. After the first week the glass form was removed daily and replaced after the vagina was irrigated. Twenty-four days after operation, the patient was discharged from the hospital, at which time the new canal was covered by an ample layer of epithelium. She was followed in the outpatient clinic, and on November 5, stilbestrol (2.5 mg. corresponding to 2,500 rat units of estrin) was given by intramuscular injection, to observe the effect, if any, on the transplanted epithelium. The same amount of stilbestrol was given on November 8, and on November 11 progynon B oleosum (10,000 international units of estrin) was injected intramuscularly. No increase in the growth

of the epithelium was noted. The patient was last seen seven months after operation. The vagina was 12 cm. long, soft and pliable, without scar tissue, and cohabitation was satisfactory. The operative result is shown in Fig. 4.

Comment

It is highly important, once the artificial vagina has been constructed, to keep it open; this must be done by normal cohabitation or by artificial dilatation. If no method of occasional dilatation is provided, even after the period of healing is over, the canal will have a tendency to become gradually smaller. This emphasizes the desirability of performing the operation only on patients who are, or are about to be, married.

Epithelization was rapid in the first few days after operation and attempts at stimulation with estrogenic substance seemed unnecessary. Later, such substances were given by intramuscular injection (Case 2) and no effect on the epithelium was noted. We may have given the estrogenic substance too late in the process of epithelization or in insufficient amounts to produce an obvious effect. One might conclude that no increase in the growth of the transplanted epithelium is to be expected, because it is not of Müllerian duct origin. It is certain, however, from the abundant evidence, that estrin is a powerful growth stimulant to the normal vaginal epithelium, which is derived from the urogenital sinus and is therefore squamous in type. Also, in the absence of estrin, following the menopause, the skin may become dry and thin as well as the vaginal mucosa. Whether or not transplanted epithelium from the skin to form an artificial vagina responds in growth to estrin is not definitely settled. At any rate, it is evident that the grafts take and grow well without giving the patient estrogenic substance. The Pyrex mold-Thiersch graft method creates a canal similar to the normal vagina in its biologic characteristics as we have shown in another communication.²³

Conclusions

There are several successful operations for the treatment of congenital absence of the vagina. We were interested in finding a safe procedure which is simple and produces a good anatomic and functional result without the growth of hair in the canal or irritating secretions. The Pyrex mold-Thiersch graft method produced such a result in the two cases herein described. The desirable psychic effect on women, after successful operation, was striking, as has been noticed by several authors. We are taking no exception to other methods of construction of an artificial vagina and the best method can be determined only by examination of the patients several years after operation.

References

1. Koff, A. K.: *The Embryology of the Female Generative Tract* in Curtis' *Obstetrics and Gynecology*, Philadelphia, 1933, W. B. Saunders Co., vol. 1, p. 572.
2. Meyer, R.: *Zentralbl. f. Gynäk.* 61: 2846, 1937.
3. Baldwin, J. F.: *Ann. Surg.* 40: 398, 1904.
4. Baldwin, J. F.: *Am. J. Obst.* 56: 636, 1907.
5. Mori, M.: *Zentralbl. f. Gynäk.* 33: 172, 1909.
6. Schubert, G.: *Zentralbl. f. Gynäk.* 35: 1017, 1911.
7. Sneguireff, W. F.: Quoted by Dannreuther, W. T.¹⁷

8. Popow, D. D.: Quoted by Meyer, J.: *Zentralbl. f. Gynäk.* 42: 639, 1918.
9. Graves, W. P.: *Gynecology*, Philadelphia, 1917, W. B. Saunders Co., p. 567.
10. Frank, R. T., and Geist, S. H.: *AM. J. OBST. & GYNEC.* 14: 712, 1927.
11. Falls, F. H.: *AM. J. OBST. & GYNEC.* 40: 906, 1940.
12. Frank, R. T.: *J. Mt. Sinai Hosp.* 7: 259, 1941.
13. Wharton, L. R.: *Ann. Surg.* 111: 1010, 1940.
14. Judin, S.: *Surg., Gynec. & Obst.* 44: 530, 1927.
15. Bodenheimer, M., and Goldman, M. L.: *J. Mt. Sinai Hosp.* 7: 310, 1941.
16. Masson, J. C.: in discussion of Falls, F. H.: *AM. J. OBST. & GYNEC.* 40: 906, 1940.
17. Dannreuther, W. T.: *AM. J. OBST. & GYNEC.* 35: 452, 1938.
18. Miller, N. F.: in discussion of Falls, F. H.: *AM. J. OBST. & GYNEC.* 40: 906, 1940.
19. Meigs, J. V.: in discussion of Dannreuther, W. T.: *AM. J. OBST. & GYNEC.* 35: 452, 1938.
20. Counsellor, V. S.: Discussion of Dannreuther, W. T.: *AM. J. OBST. & GYNEC.* 35: 452, 1938.
21. Barrows, D. N.: *AM. J. OBST. & GYNEC.* 31: 156, 1936.
22. Owens, N.: *Surgery* 12: 139, 1942.
23. Whitacre, F. E., and Wang, Y. Y.: *Surg., Gynec. & Obst.* 79: 192, 1944.

Editorial

Again, the Rh Factor*

THE obstetrician can no longer neglect to study the recent papers which deal with the complexities of the components of the Rh factor and the several varieties of anti-Rh agglutinins and their relationship to anti-Hr agglutinins. Undoubtedly, the situation is unusually baffling for obstetricians as well as for specialists in other fields. It is, therefore, desirable to read Levine's paper which appears in this issue and in which he suggests that the clinician think only in terms of the one anti-Rh serum (diagnostic'') which detects more than 90 per cent of all persons immunized either by transfusions, pregnancies, or a combination of both factors. For the study of the 8 per cent Rh⁺ mothers of erythroblastotic infants, the blood specimens should be referred to specialists in the field. In any event, it becomes essential for the obstetrician to consult frequently with the serologist for the interpretation of the findings.

Another advantage in the use of the diagnostic serum—the only one available to hospital laboratories—is the fact that it enables the obstetrician to apply a simple genetic theory, rather than the involved schemes and terminologies suggested recently.

The widespread use of blood transfusions in the past twenty years has served to immunize many Rh⁻ individuals of the female population, even as infants. Because of the long duration of the immunized state, these Rh⁻ women may be deprived of the opportunity of having one or two normal Rh⁺ infants. Certainly, precautions should now be taken to transfuse all Rh⁻ patients with Rh⁻ blood. Undoubtedly, this will be the responsibility of all physicians and especially the pediatrician. This simple measure, by itself, should reduce slightly the incidence of erythroblastosis fetalis, especially the more severe form, and also the morbidity incidental to intra-group transfusion reactions.

On theoretical grounds, the suggestion is made that with longer intervals between pregnancies and premature induction of labor, Rh⁻ mothers of erythroblastotic infants may still have an Rh⁺ infant with perhaps milder forms of the disease which can be successfully treated. It is hoped that sufficient data can be accumulated in the next few years in order to test the validity of this view.

Courses in medical genetics are gradually being introduced in the curriculum for the medical student. Powerful support for the wisdom of this step is derived from the studies on the role of the Rh factor in the pathogenesis of erythroblastosis fetalis.

*See Special Article in this issue, page 516.

American Obstetric Services

THE MARGARET HAGUE MATERNITY HOSPITAL

Jersey City, N. J.

THE Margaret Hague Maternity Hospital was built, and is operated by, the Board of Chosen Freeholders of the County of Hudson, pursuant to a special act of the Legislature of New Jersey permitting "first class" counties to so provide and operate maternity hospitals. The sole concept upon which its being is based is that the community has a responsibility in affording safe maternity care to all of its citizens of whatsoever financial capacity. Accommodations are therefore provided for both free and paying patients. The standards of essential services are uniform for all types of patients.

Situated on Clifton Place, it serves the most densely populated County of the State, with a normal population of about three-quarters of a million people, and in the thirteen and one-half years of its existence over 70,000 women have been cared for. The deficit between its receipts and its cost of operation is met out of the general tax funds of the county, this tax burden being mandatory on the County under the terms of the special act of the Legislature which established it. The hospital received its first patient on Oct. 15, 1931.

In 1940 the hospital was enlarged and completely rebuilt to permit proper organization of function in reference to the enlarged *cubage*.

The general administration resides in a Board of Managers of five members, of whom two are laymen and three are physicians as at present constituted. This Board meets regularly, and determines the broad administration policies of the hospital, subject to confirmation by the Board of Chosen Freeholders of the County of Hudson. Under its authority the executive function of the Hospital resides in a physician who functions both as Medical Director and Superintendent, with rather large discretionary powers.

The clinical work of the hospital is divided into three divisions, each headed by an Attending Obstetrician who functions as Chief of that service, being on continuous year-round service. Under broad general executive policies, each chief has autonomy relative to the details of clinical treatment and management. It is felt that this makes for a desirable diversity of practice valuable in eventual evaluation of different methods and in variety of teaching approach. Each division has a corps of from four to six assistant obstetricians. General medicine and surgery and all of their subsidiary specialties are represented by qualified members of the attending staff. The members of this auxiliary staff take an active part in consultation and the actual detailed management of clinical conditions falling within the domain of their several branches. There is a large courtesy staff, as it is felt that the hospital has a very distinct duty to the profession at large in affording the means for proper obstetric practice to the members of the profession throughout the community. The standards of practice are assured by the closest scrutiny and direction of the work of these men by the several Chiefs of Service. The house staff consists of a Chief Resident, a corps of residents, of assistant residents, and of interns. The work of all of these men and women is carefully graded so as to insure their progressive training in all phases of obstetrics. The hospital is fully approved by the American College of Surgeons, The American Medical Associa-



Fig. 1.—General view of the Margaret Hague Maternity Hospital.

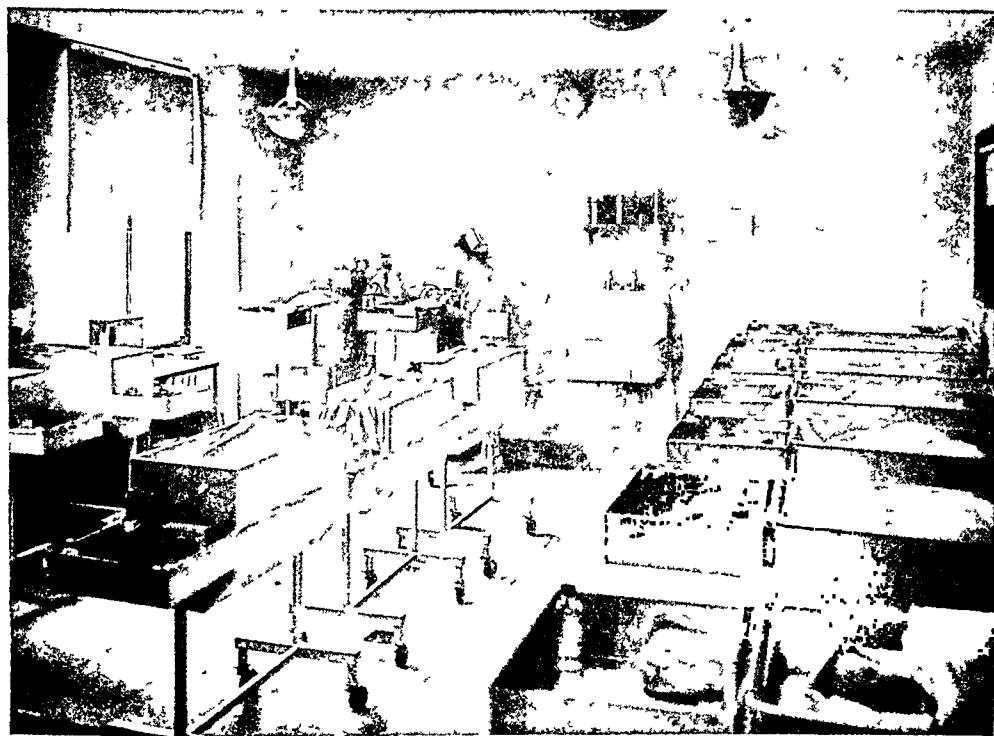


Fig. 2.—Showing arrangements in nursery.

tion, and with reference to the residencies and assistant residencies, by the American Board of Obstetrics and Gynecology.

Over one hundred contributions to medical literature have been made by members of the Staff, dealing with the work done by them in the institution.

The physical equipment is complete and modern, so departmentalized as to permit the functioning of the hospital as a completely separate and self-sufficient entity in all clinical senses. It includes facilities for nurses' training, the segregation of labor cases and cases not in labor, the complete segregation of all service to infected or potentially infected cases, complete prenatal service, abundant laboratory and x-ray facilities for all clinical needs, a blood and plasma bank, and abundant museum material, slide, library, and physical equipment for the teaching of pathology.

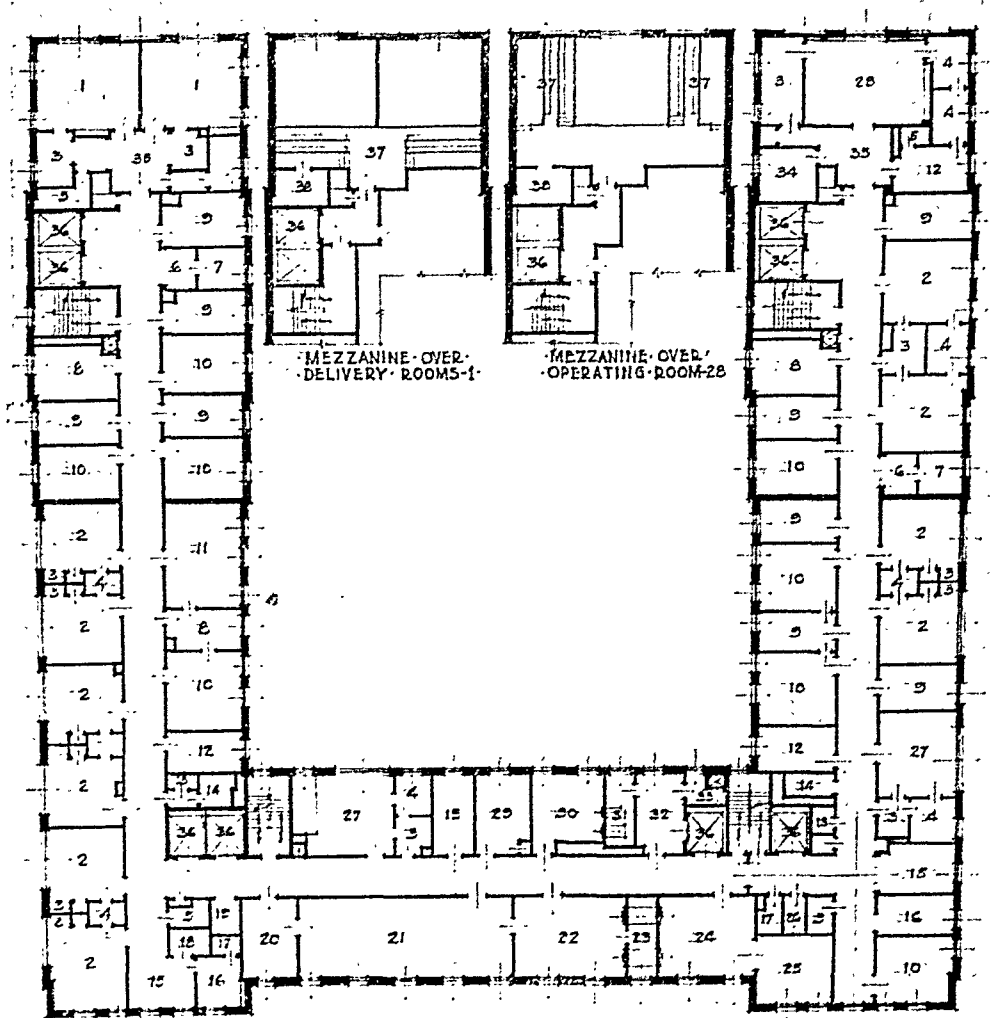


Fig. 3.—Plan of operating room floor.

- | | |
|---------------------------------|------------------------------------|
| 1, Delivery room (amphitheater) | 20, Instrument and utensil wash |
| 2, Delivery room | 21, Dressing preparation |
| 3, Surgeons' scrub-up | 22, Drum storage (unsterile) |
| 4, Sterilizer room | 23, Drum sterilizers |
| 5, Nurses' toilet | 24, Drum storage (sterile) |
| 6, Nurses' station | 25, Drum storage |
| 7, Diet kitchen | 26, Housemaids' toilet |
| 8, Nurses' workroom | 27, Operating room |
| 9, Patients' room—1 bed | 28, Operating room (amphitheater) |
| 10, Patients' room—2 bed | 29, Glove room |
| 11, Patients' room—3 bed | 30, Solution room |
| 12, Utility room | 31, Solution and glove sterilizers |
| 13, Housemaids' closet | 32, Truck and stretcher room |
| 14, Male cleaners' closet | 33, Dumbwaiter |
| 15, Nurses' office | 34, Recovery room |
| 16, Doctors' office | 35, Foyer |
| 17, Doctors' toilet | 36, Elevator |
| 18, Medicine preparation | 37, Observation gallery |
| 19, Stretcher closet | 38, Storage and coat room |

The building is completely separated from all other units, except for an underground tunnel which connects it with other units of the Jersey City Medical Center.

The largest adult bed units are four-bed "wards."

Each floor nursery has a total capacity of about 60 bassinets. They are divided into three units which can be separately operated if necessary. There is also, in connection with each, a separate "observation" nursery. The latter, as well as the main "septic floor" nursery, is cubicled for maintenance of proper isolation technique.

The hospital is affiliated for graduate teaching of obstetrics with the University Extension Division of Columbia University. The hospital is affiliated with, and forms a part of, the Jersey City Medical Center, and close affiliation is maintained with the gynecologic tuberculosis, and other special and general services of that institution.

A well-organized school of nursing in obstetrics is maintained. Students consist of three groups: undergraduate affiliates, postgraduate students, and postgraduate special students pursuing extended training in ward management and supervision.

SUMMARIZED STATISTICS FOR THE FIVE YEARS, 1939 TO 1943, INCLUSIVE

Total number of beds	345	
Admissions	36,590	
Live births	30,844	
Mortality:		
Maternal	65	(0.21 per cent)
Fetal	730	(2.36 per cent)
<i>Residents, Interns, and Postgraduates</i>		
Interns	852	
Residents	66	
Ass't residents	2	
Postgraduates (3 months)	110	
Postgraduates (1 month)	27	
	<hr/>	1,057
<i>Medical Students, New York Medical College</i>	112	
	<hr/>	1,169
<i>Postgraduate Students, Nurses</i>		
Total enrollment, Dec. 3, 1931, through 1943	1,153	
Incomplete	118	
	<hr/>	1,035
<i>Affiliate Nursing Students (Representing 9 schools)</i>		
Total enrollment, Oct. 22, 1931, through July 31, 1944	1,353	

S. A. COSGROVE, M.D.
Medical Director and Superintendent

Department of Statistics

ANALYSIS OF MORTALITIES FOLLOWING EXCISION OF THE UTERUS AT THE PHILADELPHIA GENERAL HOSPITAL, 1931 TO 1941 INCLUSIVE*

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(From the Gynecological Division of the Philadelphia General Hospital)

IN 1931, the gynecologic and obstetric staff at the Philadelphia General Hospital began a discussion at the end of each chief's service of the morbidities and mortalities of that term.

As the years have gone by, much constructive criticism was offered in these conferences. The reviews, however, were of rather short series of cases, but were of benefit because each individual death was carefully analyzed. It has seemed that a review of the mortality following one particular phase of our operative procedures would be of interest to the Society. During the years 1931 to 1941, the staff had eight chiefs, each with two or three assistants on rotating services so that the series of cases to be presented has spread throughout a large number of operators. Some cases have been recorded from a clinical standpoint, but, at no time, have our failures been collectively presented.

TABLE I. GYNECOLOGIC MORTALITY RATES

	NO.	DEATHS	MORTALITY RATE
Admissions	14,104	318	2.25
Women operated	6,372	150	2.35
Abdominal operations	2,876	103	3.56
Abdominal hysterectomies	1,870	52	2.77
Vaginal hysterectomies	88	1	1.13

During the period, 1931 to 1941 inclusive, 14,104 women were admitted to the gynecologic wards of the hospital. Of these 318 died, a mortality rate of 2.25 for the service; 6,372 women were operated on with 150 deaths, a mortality rate of 2.35. There were 2,876 laparotomies with 103 deaths, a mortality rate of 3.56. In the latter group, the uterus was removed in 1,870 cases for various indications. Of this number 52 died, a mortality rate of 2.77. The uterus was removed in 88 other cases by vaginal route with one death, a mortality rate of 1.13.

TABLE II. INDICATIONS FOR ABDOMINAL HYSTERECTOMIES

	SUBTOTAL		TOTAL	
	MORTALITY RATE: 2.48		MORTALITY RATE: 6.38	
	NO.	DIED	NO.	DIED
Tumors	1,345	36	103	8
Residues	269	5	24	0
Adnexal diseases other than inflammatory diseases	53	0	1	0
Ectopic pregnancy	34	2	1	0
Endometriosis	12	0	2	0
Miscellaneous	16	0	10	1
Total	1,729	43	141	9

*Read at a meeting of the Obstetrical Society of Philadelphia, May 4, 1944.

The indications for the abdominal hysterectomies appear in Table II. They have been grouped according to operative diagnosis or pathologic reports as tumors; residues of inflammatory conditions; adnexal disease, other than infection and inflammation; ectopic pregnancy; endometriosis; and a miscellaneous group in which several indications were, indeed, bizarre.

Vaginal hysterectomies were performed, as will be seen in Table III, for uterine descensus, procidentia, uterus partly or entirely extruded, fibroid, cystocele, cervicitis, abortion and retroversion.

TABLE III. INDICATIONS FOR VAGINAL HYSTERECTOMIES

	NO.	DIED
Prolapsed uterus	36	0
Procidentia	25	1
Fibroid	10	0
Cystocele	6	0
Cervicitis	4	0
Abortion	3	0
Retroversion	4	0
Total	88	1

The operative procedures in the abdominal hysterectomies are shown in Table IV. This includes both the subtotal and complete hysterectomies. The operative procedures in the vaginal hysterectomies are shown in Table V.

TABLE IV. OPERATIVE PROCEDURES IN ABDOMINAL HYSTERECTOMY

Hysterectomy only	638
Hysterectomy, both tubes and ovaries	891
Hysterectomy, one tube and ovary	239
Hysterectomy, additional operations	102

TABLE V. OPERATIVE PROCEDURES IN VAGINAL HYSTERECTOMY

Vaginal hysterectomy only	60
Vaginal plastic	24
Dilatation and curettage	2
Left salpingo-oophorectomy and appendectomy	1
Salpingectomy	1

In an article by John Osborne Polak,¹ he posed the question: "What Can We Learn From a Study of Mortalities?" In this review of the work at the Long Island College Hospital, he discussed their routine procedure and detailed the following minimum preoperative requisites for all elective sections, namely:

1. A complete history and general physical examination.
2. A leucocyte count of between 7,000 and 10,000.
3. A polymorphonuclear percentage of from 65 to 80.
4. A hemoglobin of at least 60 per cent.
5. A sedimentation time of 90 minutes or more.
6. A normal urinalysis, and an adequate kidney function.
7. A temperature of 98.6° F. for at least 48 hours before operation.
8. A systolic blood pressure between 110 and 150.
9. A negative Wassermann test, and finally, that all elective preoperative patients have rest in bed in the hospital for a period of at least 48 hours, during which time the intake of fluids, water, milk, etc., must be at least two and one-half quarts per diem, while the usual sugar intake of the individual must be at least quadrupled.

This list of minimum preoperative requisites was posted at the intern's desk in my gynecologic ward and I tried to have it followed,

but with many acknowledged lapses, while on service each year. I was impressed in Polak's study of his mortalities by the finding that the fatal issues reported could be attributed in a high proportion to an omission or misinterpretation of history, physical examination or laboratory procedure, or disregard of some important preoperative requisite.

Polak mentioned, too, as factors in mortality the high Trendelenburg position in hypertensives producing a cardiac embarrassment and the prolonged Trendelenburg in hypotensives predisposing to the occurrence of shock. He commented, too, on the amount of surgery done at one sitting or overreaching the maximum of safety in time consumed in operation. He particularly pointed out the necessity of preoperative bed rest, and the avoidance of operation in any case showing low grade as well as active infection. Polak evidently did not favor routine removal of the appendix during pelvic operation.

In recent years, much attention has been paid to the nutrition of the patient as a prerequisite for surgery. Probably this might be of more importance in general surgery, particularly of the intestinal or biliary regions, than in pelvic surgery. Nevertheless, the well-nourished patient withstands operation of any nature better than the debilitated one. Blood serum protein level of eight milligrams per cent is generally regarded as an index of a favorable nutritional status preceding surgery.

I have considered comparing the records of the patients who died having in mind Polak's list of prerequisites, but felt such a comparison should be delayed until sufficient time had elapsed to obtain a sample large enough to be of interest.

In reviewing the histories and physical examinations of the 53 women under discussion, it is at once admitted that every woman had a history and a physical examination. The quality of some of the histories, even in recent years, not infrequently indicated a rather sketchy statement of the symptomatology. The history or the physical findings on admission were frequently at variance with statements made after the operation had been performed. This was particularly true with regard to cardiac status. In this respect, I tried to safeguard my service by endeavoring to have the interns use the history forms proposed by Ward in the Woman's Hospital in New York, but, as the form was not printed on our history sheet, this historical and regional sequence was not always followed.

History and physical examination of these 53 patients, who died, are of particular interest with regard to the history of finding of cardio-circulatory diseases. (We have one with a history of arteriosclerosis, four with a history of hypertension, one with a history of cardiovascular disease. Two were labeled as having "arteriosclerotic hearts," one as myocardial disease, one with rheumatic heart disease, two with heart disease unspecified, and two with mitral disease.) Practically one-third had cardiac or vascular lesions.

If we turn to the subject of the white blood cell count as indicative of prolonged subacute or chronic infection, even in the case of an apparently well ambulatory patient, we find no record in eleven of the 53 histories. In 24, or nearly one-half of the cases, the leucocytes ranged between 7,000 and 10,000. There were 16 cases in which the count was above 10,000. Six of these cases died of peritonitis following operation, and six died of cardiac failure. In the two women whose leucocyte count was below 7,000, one died of shock, and the other was regarded as having had a cardiac collapse, although peritonitis was indubitably the terminal causative factor. One woman who was admitted to the hospital with a leucocyte count of 22,000 had a preoperative stay of 32 days. The last recorded leucocyte count, 18,560, was taken seven days before her hysterectomy. She died of pulmonary embolus following a thrombophlebitis of the iliac veins.

With regard to the differential count of the white cells, there is no record in eleven histories. Twenty-two women had counts between 65 to 80 polymorphonuclears. In twelve the percentage was less than 65, and in eight the percentage was above 80. In this latter group, six died of infection, peritonitis, and another of pneumonia.

Only 13 hemoglobin estimations were recorded in 53 histories. Consequently, a discussion of anemia in connection with these fatalities must necessarily be based on the 45 instances in which red blood counts were made preoperatively. If we consider a red cell count of 3,000,000 or lower, in the absence of hemoglobin estimations, as determining anemia, with its consequent lessened resistance we find ten cases with counts below 3,000,000 and five additional cases with counts below $3\frac{1}{2}$ million. The influence of these anemias is reflected in the fact that eleven deaths in this group resulted from infection.

Sedimentation time was estimated on 35 cases in the series. According to the technique used, 20 were regarded as rapid. Of these eleven died from peritonitis following the operation. (In two further cases death resulted from pneumonia.)

Examinations of urine revealed albumin estimated at + to +++ in 20 instances, while in five additional instances, the presence of casts in the urine in the preoperative period is noted.

Sugar was present in preoperative specimens in three instances. There is no mention in the three histories that standardization of the diabetes had been carried out preoperatively. Two additional cases, where the glycosuria was first discovered postoperatively, had blood sugar estimations of 186 and 224. Two of the three patients, who had sugar in the urine preoperatively, had no estimations of the blood sugar while the third case had a preoperative blood sugar of 160. One of these patients died of shock, the others of peritonitis.

With regard to nitrogen retention, 12 records show a blood urea nitrogen of 16 or above, indicating a certain degree of renal damage or renal dysfunction or dehydration. The deaths in this group resulted equally from cardiocirculatory causes and infection.

The significance of low grade temperature preoperatively was stressed by Polak. He advised that in such cases operation should be postponed until the temperature reached normal, and had remained so for several days. In this series, 29 had temperatures of 99.2° F. or above, within 48 hours before operation. Of the 29, ten had temperatures of 100.2° F. or higher, in the same preoperative period. Peritonitis was the outstanding cause of death in this group.

A negative Wassermann test was regarded by Polak as an essential for an elective operation. I believe it has been felt, in the years subsequent to his paper, that syphilis plays little, if any, part in postoperative morbidity or mortality. (There were seven positive Wassermann cases, 20 per cent of such tests made. It is interesting that none of the seven positive reactions occurred in the hypertensive cases.)

In this series, there were 16 women whose blood pressure was above 150 systolic, a reading Polak gave as a minimum high point for safety in elective operations. (There were two whose pressures were less than 110 systolic.) Eight of the first group had systolic pressures from 150 to 180, and in eight the range was from 180 to 230. Five of the 16 had cardiocirculatory failure deaths. (The two highest diastolic pressures were 130 and 140. It is evident that these diastolic pressures were not actively concerned in the death, for each woman died of peritonitis; one of the diffuse type and one of the ileus type.)

In so far as bed rest in the hospital before operation is concerned, it must be remembered that the Philadelphia General Hospital, being a free service institution, is not concerned, for the most part, with a very rapid turnover of patients, and women may be held for rest in bed as long as necessary to prepare them for operation. Four women were operated on the day following their admissions. Of these, three died of

peritonitis, and one of shock. Four patients were operated on within 48 hours after their admission. Of these patients, two died of cardiac failure, one of hemorrhage and one of peritonitis.

Operative Risk

The summation of history, physical examination, pelvic findings and preoperative clinical course determines the evaluation of a woman as an operative risk. Seven records disclose a statement that the patient was a poor risk, sixteen times a doubt is expressed in the term "fair risk." Twenty were regarded as good risks; in the remaining ten, no statement is found. It was difficult to determine on many charts whether these notes, as to risk, referred to anesthesia or operation.

In but a small percentage of these records was any statement as to the need for operation. The pathology present, as described in the pelvic examination, seems to have bluntly indicated why an operation was to be done.

Jellett² has concisely summed up this topic. He says: "The principles relating to the necessity for operation are comparatively simple. A proposed operation is either essential or advisable; essential in that if it is not done the patient will in all probability die; advisable in that it will benefit the comfort or health of the patient. An operation may be essential, but still may not be possible owing to the state of the disease, or it may be essential and at the same time involve such risks owing to the patient's state of health that the chances of benefit are remote."

"A necessary operation to be permissible must not involve a greater risk to the patient than does the condition for which it is performed. An advisable operation, to be justifiable, must only possess risks that are negligible in comparison with the benefits that are likely to follow it."

Anesthesia

Ether was the anesthetic of choice, being used in 39 patients. In 17 of these, gas induction was used. Spinal anesthesia was used eleven times, ether was used as a supplement in three. In three cases cyclopropane was the anesthetic agent.

All the pneumonia deaths followed the use of ether. Although the association may have been an accidental coincidence, it is nevertheless, noteworthy. One anesthetic death occurred during the use of ether. Three of the five shock deaths followed the use of spinal anesthesia. Preoperative sedation, barbiturates and morphine rather than ether predisposed to the death of the one vaginal hysterectomy case.

Length of Operation

Just what constitutes a safe duration of time in performing an hysterectomy is a difficult question to answer. The time must depend upon the nature and extent of pathology in the principal, as well as in the associated, lesions, and upon the ability and experience of the operator.

The average time in 42 cases, where the time of operation was recorded, was one hour and 35 minutes. Eighteen operations consumed almost exactly this time. Only four operations were performed in an hour or less. In nine abdominal cases the operating time was two hours or more, of these, three were total hysterectomies. Six had myomas, two ovarian cysts, and one a residual inflammation of the adnexa. Six died of peritonitis, two of cardiocirculatory disease and one of cerebral embolus.

The mortality in the hysterectomies done at the hospital during these 12 years varies widely according to operative procedure. Where only the uterus was removed the mortality was under one per cent (638—5). Where either both tubes and ovaries, or one tube and ovary was removed with the uterus, the mortality jumped to 3.1 and 3.3 per cent, respectively (891—28 and 239—8).

In 102 cases where other operations were combined with hysterectomy, with or without unilateral or bilateral salpingo-oophorectomy, the mortality (11 deaths) was 10 per cent. In all but a few of these 102 cases, the appendix was removed. In this mortality group, peritonitis was the cause of death in eight. The high mortality may be taken as indicating more extensive pathology than in the other groups, a greater degree of tissue trauma, too extensive surgery or infection arising from the appendiceal stump.

A few remarks might be made upon each of the eight headings in the causes of death. (Table VI.)

TABLE VI. CAUSES OF DEATH

	SUBTOTAL	TOTAL	VAGINAL
Anesthesia (died on table)	1		
Surgical shock	5		
Hemorrhage	3	1	
Embolus	4		
Peritonitis	18	6	
Cardiac-circulatory	7	1	1
Intestinal obstruction	1		
Pneumonia	4	1	
Total	43	9	1

Anesthesia

The one death during anesthesia occurred in a 45-year-old multipara vi, a Negro woman, operated upon for a large myoma producing pain. She complained, in addition, of dyspnea, ankle edema and weight loss, blood pressure was 170/100 and heart was found markedly enlarged, with some myocardia degeneration. The anesthesia, open ether, was received badly and not withstanding forced oxygen and CO₂ inhalations, the patient died as the operation ended. There was no pathologic report found, but the notes of the surgical findings state that there was some adnexal inflammation. The latter may have accounted for the 10,000 leucocytes, only count made, and temperature over 99 within 48 hours before operation.

Shock

Five cases, all operated for myoma, died of shock. One or more of these showed age of 60, leucocytosis above 10,000, rapid sedimentation time, hypertension, low hemoglobin estimation, low erythrocyte count, glycosuria, operated upon within 24 hours after admission, blood urea nitrogen of 20 mg. per cent and albuminuria. Three were regarded as poor risks, one as a fair risk, and no statement found in the last history. There can be little doubt that these five women were poor prospects for major abdominal surgery.

Hemorrhage

Four women died of hemorrhage. All had preoperative diagnosis of myoma. The first had, in addition to the myoma, an old ectopic pregnancy. After hysterectomy and partial removal of the ectopic mass, the sac was marsupialized and packed. Hemorrhage of a fatal degree followed removal of the pack.

Two of the remaining patients died within 24 hours and the fourth died on the third day after operation. Massive intra-abdominal hemorrhage occurred in two, and the other patient who had a pelvic gauze pack bled slowly but fatally, dying on the third postoperative day.

It is difficult to ascribe these deaths to any lack of preoperative requisites. There were two autopsies in this group.

Embolus

There were four deaths from embolus. In only one operation was the clamp technique used. In all of them the preoperative diagnosis was

myoma. The deaths occurred on the sixth, tenth, eleventh and thirteenth days after operation. One embolus, evidently arose from a thrombophlebitis of the iliac veins. In another, appendectomy followed an apparently routine hysterectomy. The appendix was buried in fat. Its removal was difficult and much ligation of bleeding areas was necessary. A final note by an intern advances the possibility that the appendix area was the originating point of the total pulmonary embolus.

One embolic death, following a total hysterectomy with a laboratory diagnosis of adenocarcinoma, was preceded a few hours by a numbness in the foot and subsequent muscular weakness in the leg. Death occurred the same day.

The fourth death in this group may have been a cerebral embolus or a right cerebral thrombus. The death occurred on the thirteenth day. The postoperative course had not been a septic one, and there was no hypertension. Preoperative requisites here had been well met, except for blood studies. The operating time was just over two hours, routine subtotal hysterectomy, alone for myoma. There were no autopsies in this group.

Peritonitis

There were 24 deaths from peritonitis; 18 in the subtotal and six in the total type of operation. In the group of indications termed residues, which included all inflammatory conditions of the adnexa as the chief filing diagnosis, there were five deaths, all due to peritonitis. It is probable in the case where myoma was the filing diagnosis and death resulted from peritonitis, that some residual foci of previous infection in the adnexa may have contributed to the fatal outcome.

In a group of subtotal hysterectomies, mostly with removal of both tubes and ovaries, in which death resulted from peritonitis, preoperative requisites were largely disregarded. In one or another case, there were recorded high leucocyte counts, low erythrocyte counts, high polymorphonuclear counts, preoperative fever, one-day bed rest only before operation, prolonged operating time, one operation followed in two days a colpotomy to determine the nature of a pelvic mass, hypertension, elevated urea nitrogen, and removal of appendix with an oozing pelvic cavity which necessitated a gauze pack. In two of the total hysterectomies where death resulted from peritonitis, no vaginal antisepsis had been carried out. It was stated that in one operation the vagina was opened inadvertently and a total operation was necessitated.

In almost the entire group of infection deaths, a closer analysis of the case findings and a more critical evaluation of the operative risk must have been of benefit.

The diffuse type of peritonitis occurred in a ratio of about two to one in relation to what was referred to in the histories as the ileus type of peritonitis. It is noteworthy that in three cases where the cause of death was given as paralytic ileus, definite peritonitis was found at autopsy.

Cardiocirculatory Disease

The nine deaths in this group were divided in seven myoma cases, one noninflammatory adnexal lesion (large cyst), and one prolapse of the uterus, a vaginal hysterectomy. From the cardiac standpoint, two patients had hypertension, blood pressures of 160/110 and 180/100; a third had an enlarged heart with myocardial degeneration and a blood pressure of 176/90. In the other histories, no definite lesions of the heart are recorded. The deaths in this group occurred from the second to seventh days. The patients were not febrile, postoperatively, were not recorded as having had an unusual operative blood loss, but had not met the preoperative requisites in anything like a perfect score. It is interesting to read the similarity of intern's progress notes made on histories as long as ten years apart. "Patient did not recover well after operation, heart seemed played out, pulse grew weaker, patient died."

This describes most of the group. Possibly this group represents individual inability to withstand operation. Possibly some may have been too undernourished to recover from the brunt of visceral manipulation.

Intestinal Obstruction

Although more than one of the ileus type of peritonitis deaths may actually have been intestinal obstructions, there was one case definitely due to this cause. The preoperative and filing diagnoses were myoma. Both tubes and ovaries were removed with the uterus. The preoperative findings included a leucocytosis, fever and a rapid sedimentation time. There was a typical obstruction picture from the fifth to the ninth days, with postmortem findings of ileum adherent to the cervical stump.

Pneumonia

In four patients operated on for myoma and in one operated on for residues, death resulted from lobar pneumonia in two, and bronchopneumonia in three. There were a number of cases of bronchopneumonia recorded as having occurred during the course of a fatal peritonitis; they were regarded as secondary lesions. In these pneumonia deaths, either had been the anesthetic. Lobar pneumonia developed in both instances seven days after operation in otherwise uncomplicated convalescences. The bronchopneumonia cases both followed instances where difficulty was experienced in administering the anesthetic. In one case the laryngoscope was passed during the operation. In the other, vomiting occurred during the inhalation ether anesthesia. Autopsy confirmed the diagnosis in two cases, and roentgen examination in the third.

Probably cases with perfect preoperative findings, and in excellent physical condition, might have developed similar fatal lesions. Yet, deficiencies in requisites in some respects suggest lowered resistance on one hand, and poor anesthetic risks on the other.

A review is presented of the mortalities following excision of the uterus over an eleven-year period. The indication for these operations are shown. The preoperative status of the women who died has been compared with a not too exacting set of preoperative requisites for elective gynecologic operations. The deaths have been discussed in groups by indication for operation and by causes of death.

The literature of the subject indicates a lower mortality following excision of the uterus in clinics where the staff on a continuous service has one directing head, and where a uniformity of procedure for preoperative requisites, operative technique, and postoperative treatment is closely adhered to by all operators.

With a large and loosely united staff, on short terms of service, with multiple systems of procedures, a set of standing orders for operative cases, mutually agreed upon, and covering, at least, preoperative requisites and postoperative treatment should help to lower morbidity and mortality, lessen nursing problems, and unify the training of interns and residents.

References

1. Polak, J. O., and Tollefson, D. G.: *Gynecological Transactions* 53: 169, 1928.
2. Jellett, H.: *Gynecology*, Philadelphia, 1925, Lea & Febiger, p. 436.

Special Article

RECENT DEVELOPMENTS IN ISO-IMMUNIZATION BY THE RH FACTOR

PHILIP LEVINE, M.D., LINDEN, N. J.

(From the Ortho Research Foundation)

THE observation in 1939 that fetal blood may immunize the mother—in the same way, for example, that male patients may be immunized by repeated blood transfusions—paved the way for the description of the pathogenesis of erythroblastosis fetalis.¹ In a series of papers (1941 to 1942),²⁻⁴ evidence was produced to show that (1) erythroblastosis fetalis is the result of prolonged intrauterine reaction of maternal immune agglutinins and susceptible fetal blood, (2) at least 90 per cent of all mothers of erythroblastotic infants are Rh- and their husbands and the affected infants are Rh+, (3) in the smaller group of Rh+ mothers, finer differences within the Rh complex as well as several other blood factors other than Rh (such as the blood factor of Levine and Polayes, Hr, A, B, and perhaps others) may be responsible for iso-immunization of the mother, (4) Rh- immunized mothers can be safely transfused with Rh- blood, and (5) the chances for survival of the affected Rh+ infants of Rh- mothers are better if they are transfused with Rh- blood.

Curiously enough, the presence of anti-Rh agglutinins, which is direct proof of immunization, could be demonstrated only in about 50 per cent of the Rh- mothers even if tested soon after delivery.³ This difficulty has now been met with the demonstration independently by Race⁵ in England and Wiener⁶ that many Rh- mothers of erythroblastotic infants have anti-Rh antibodies which specifically unite with and coat the surface of Rh+ blood, without inducing the visible effect of agglutination. In other words, the antibody is incomplete because only the first stage of the reaction, i.e., specific union, occurs. The specifically coated Rh+ blood is now incapable of reacting with potent anti-Rh agglutinins. Accordingly, Wiener called these "blocking" antibodies while Race used the term "incomplete" antibodies. These significant findings were soon confirmed by several workers (Diamond, Fisk and Morrow, and Levine). At any rate, it is certain that in vivo the specific reaction goes to completion so that the end result is hemolysis. In other words, clinically, one cannot differentiate erythroblastotic infants of mothers who have anti-Rh agglutinins from those whose mothers have the incomplete antibody. By the same token, both groups of mothers are subject to severe and even fatal hemolytic reactions if they are transfused with Rh+ blood.

Early in the work on transfusion reactions and on erythroblastosis fetalis, it was observed that not all anti-Rh agglutinins are of identical specificity.⁷⁻⁹ This difficulty was soon solved when it could be shown that a particular anti-Rh serum, containing but one agglutinin acting on 85 per cent of all white individuals, gave the highest value of Rh- reactions among the mothers of erythroblastotic infants.^{8, 10} Levine² recommended a single genetic theory in order to explain the contrasting obstetric histories, i.e., either repeated or sporadic

fetal and neonatal morbidity. In the former instance, the father is homozygous (RhRh) for the Rh factor, while in the latter he is heterozygous (Rhrh).

The varieties of anti-Rh sera indicated a complex or mosaic structure of the Rh factor, but no attempt was made to present the serologic details to clinicians since one serum alone served as a diagnostic reagent to detect more than 90 per cent of all individuals immunized by either pregnancy or, by the same token, repeated blood transfusions.

Wiener,¹¹ in an effort to elucidate the genetic theory of the Rh complex, proposed a terminology and in rapid succession several modifications thereof. At the same time, the British workers, Race¹² and Murray,¹³ suggested at least two alternative terminologies so that the present situation is utterly confusing, not only to clinicians but also to immunologists and geneticists. Very briefly stated, Levine and his co-workers had shown that two common varieties of human anti-Rh sera describe four types of bloods.^{3, 8, 9} Later, Race¹⁴ and Wiener¹⁵ described a third variety which agglutinates the blood of 30 per cent of white individuals. This serum further divides the four types, thus making eight subtypes. Fortunately, as will be shown below, it is wiser and safer for the obstetrician and clinician to consider only the clinically most important variety which gives 85 per cent reactions in a random white population. From a practical standpoint, he must know whether his patient is Rh+ or Rh- with this serum. For this reason, it becomes necessary to identify it, and the writer would like to suggest the term "diagnostic" anti-Rh serum.

Further support for the prominent role of the "diagnostic" anti-Rh is derived from the direct correlation of Rh- individuals in several races studied and the incidence of erythroblastosis fetalis.^{8, 16} Erythroblastosis fetalis is almost unknown among Chinese, because instead of 15 per cent of Rh- individuals, as in the white race, the value among Chinese is less than 1 per cent. Such correlations cannot be obtained in corresponding studies with other varieties of anti-Rh sera.

For the exceptional 8 per cent† of the mothers who are Rh+, it is necessary for the clinician to refer the blood specimen to serologic specialists in the field. Evidence for iso-immunization in these cases can be obtained by tests with (1) blood grouping sera, (2) two other varieties of anti-Rh sera reacting with 70 per cent and 30 per cent, respectively, of white individuals, (3) anti-Hr serum,¹⁷ and rarely, still other sera. The report in these cases can be stated as an incompatibility either of a particular blood property or due to finer differences of the Rh factor. Accordingly, it seems unnecessary, at least for the present, to urge the clinician to commit to memory a series of complex terminologies, especially when his own laboratory will have only the diagnostic serum for testing.

Until all varieties of anti-Rh sera become generally available to hospital laboratories, one may expect a very occasional intra-group transfusion accident due to iso-immunization by the Hr factor or by finer differences of the Rh factor. The rule in these cases is to select donors of the same subtypes as the immunized patient. By the same token, the erythroblastotic infants of Rh+ mothers should receive transfusions of compatible blood of the same subtype as the mother. In general, mother's blood, if incompatible, may be used for her affected infant

*This term is preferable to "standard" anti-Rh sera which refers to the experimental serum of Landsteiner and Wiener. Since this serum did not give satisfactory agglutination reactions, it was not clear whether or not it contained more than one antibody.

†The initial value of 10 per cent can probably be lowered by 2 per cent, for, in practically all cases in which the diagnosis of erythroblastosis fetalis is in doubt, the mother is Rh+. In one of Dr. Burnham's cases, it was later shown that the infant had Mediterranean (Cooley's) anemia with onset of symptoms in the neonatal period.

provided that the plasma be removed and replaced with saline or compatible plasma.

Actually, all blood specimens in selected cases (fetal and neonatal morbidity, complications of pregnancy, and intra-group transfusions reactions) should be subjected to intensive studies with all varieties of agglutinins. Since this cannot be carried out in the average hospital laboratory, the same material should be sent to qualified workers for a more intensive evaluation such as standardization of anti-Rh or other agglutinins, blocking or incomplete antibodies, and various titrations. If potent anti-Hr sera are available, tests should be made for the selection of these Rh+ fathers of erythroblastotic infants who are homozygous.^{10, 18} The bloods of these individuals lack the Hr factor, and will, therefore, not be clumped by potent anti-Hr sera. The intensive study of this vast selected material should result in an increase in the supply of anti-Rh sera of all varieties. Certainly, every obstetrician is aware of the current difficulty in meeting the demands of hospital laboratories for the "diagnostic" anti-Rh serum. The situation will be much relieved as soon as potent anti-Rh sera can be produced in the experimental animal.

Obviously, it is important to determine the exact genetic behavior of the several Rh genes, but a complete theory cannot be offered unless potent specimens of the rare reagents, one variety of anti-Rh serum (30 per cent reaction in white) and the anti-Hr serum become available. Only then will it be possible to accumulate data on complete family and racial studies, the analysis of which should yield the correct genetic theory. Large scale investigations are essential since some of the subtypes are exceedingly rare.

The widespread publication of genetic schemes and terminologies for the numerous subtypes gives the clinician the wrong impression that bloods can, at all times, be classified in terms of this terminology. The fact is, however, that not even the several serologists active in this field have a constant supply of the necessary reagents for the differentiation of the several varieties of Rh+ and Rh- blood.

Undoubtedly, in time it may become necessary to adopt one of the several varieties of terminologies, but this should be decided upon preferably by an international committee as was done in the case of the four blood groups. Meanwhile, the isolated expert will perforce continue to use one of the terminologies in his own studies. However, his report to the clinician on the group of Rh+ mothers can be worded as incompatibilities detected by particular anti-Rh sera, anti-Hr sera, or blood grouping sera. Under such an arrangement, the clinician need not trouble himself with the identification of the particular variety of Rh+ and Rh- blood.

As indicated above, one may recommend to the clinician a simple genetic theory based on the behavior of the diagnostic serum, which contains but a single antibody. Accordingly, there are three genotypes, RhRh (homozygous), Rhrh (heterozygous), and rhrh (recessive). The first two represent Rh+ bloods which cannot be differentiated with anti-Rh sera. However, the Rh+ individual whose blood is not agglutinated by anti-Hr sera is homozygous for the Rh factor. A more detailed analysis which requires the use of other anti-Rh sera can be supplied by the serologic specialist.¹⁰

In the past three years it has become increasingly clear that once an Rh- individual is immunized, either by repeated transfusions or by pregnancies, he or she must be considered as remaining immunized for the remainder of his or her natural lifetime.¹⁹ Thus, a woman who delivered an erythroblastotic in-

fant eleven years previously has tolerated one transfusion of Rh+ blood, but the following transfusion with Rh+ blood resulted in a violent reaction and anuria. By the same token, an Rh- woman was deprived of an opportunity of having one or two normal Rh+ children because, as a child of 6 years, she was already immunized by several blood transfusions. It is significant that in this case the first born had the most severe form of erythroblastosis fetalis, i.e., fetal hydrops. Several cases of this sort observed recently will be published in the near future.²⁰ Accordingly, it is necessary to consider the advisability of introducing in pediatrics the routine practice of carrying out Rh tests in all female patients to be transfused. In transfusing an Rh- female infant, it is essential to keep in mind her future pregnancies. In a broader sense, no girl or woman, regardless of age, should be transferred unless tests for Rh are carried out. Those found to be Rh- must receive only Rh- blood. With the availability of larger amounts of anti-Rh sera, such tests could be carried out in all cases, but in instances of repeated transfusions in the absence of pregnancy there is always a warning symptom of safety, i.e., a severe chill or slight jaundice which should serve as a definite indication to carry out Rh tests before another transfusion is given.

In the several reviews of the subject, no mention is made of the most significant fact that erythroblastosis fetalis establishes a precedent for fetal or neonatal morbidity attributable to a difference in a blood factor which has a normal distribution in any race. Since the blood factors involved are inherited, erythroblastosis fetalis can be considered as a disease due to genetic and constitutional causes. There already is some evidence that the antigenic factors in fetal blood other than Rh, such as A and B, may also immunize the mother with the end result of fetal and neonatal morbidity other than erythroblastosis fetalis.^{21, 22}

From the very beginning of his studies, the author has stressed that the same statistical approach can be applied to any complications of pregnancy and the neonatal period.²³ Recently, Yannet²⁴ and Snyder²⁵ observed a somewhat greater incidence of Rh- reactions among 122 mothers of feeble-minded infants. Further studies are required to elucidate the relationship of this group of feeble-mindedness to kernicterus.

As for the mechanism of iso-immunization, it is thought that unbelievably minute amounts of fetal red blood cells in one form or another find their way into the maternal circulation in every normal pregnancy.¹⁹ Iso-immunization occurs, however, in only a small proportion of Rh- women whose husbands are Rh+. The obstetrician is in the strategic position of being able to reassure those Rh- women who have become unduly alarmed as a result of incomplete information acquired from popular accounts in newspapers and magazines. The Rh- woman should be instructed that most of them can have two or more normal infants before they become sufficiently immunized to have an erythroblastotic infant. There is sufficient evidence to support a statement that the chances for survival of the affected infants are much better at present because the condition can be anticipated and treatment instituted promptly.

Although the silent process of iso-immunization by the fetus cannot be controlled, nevertheless the outlook for Rh- women is now much better than previously. In the first place, one can prevent the deliberate iso-immunization of the Rh- female population by transfusions with R+ blood.²⁶ Secondly, the blood of the pregnant Rh+ woman should be tested periodically to detect the earliest onset of iso-immunization. In general, failure to demonstrate antibodies throughout the pregnancy make it possible to give a good prognosis. If

antibodies are present and on the increase, the physician can make the diagnosis of erythroblastosis fetalis well in advance of the delivery. Premature induction of labor in selected cases in order to shorten the period of intrauterine hemolysis seems a logical procedure, but its value is still to be determined. At any rate, the affected infant should be transfused immediately with random Rh- blood via the cord vein as suggested by Mayes.²⁷ No further pregnancies should be recommended until after the disappearance of all residual agglutinins or incomplete antibodies produced in the previous pregnancy. In addition to this, another interval of one or more years should elapse before another pregnancy is attempted. In this manner, it is hoped to reduce the intensity of the iso-immunization in the following pregnancy. In all cases, complete blood studies of the mother, father, and surviving children, if any, should be carried out. This will make it possible to determine the genotype of the father, whether homozygous or heterozygous.

Finally, organized effort should be directed toward the training of qualified laboratory workers in the theoretical as well as practical aspects of this new and clinically important field of medicine.

References

1. Levine, P., and Stetson, R. E.: *J. A. M. A.* 113: 126, 1939.
2. Levine, P., Katzin, E. M., and Burnham, L.: *J. A. M. A.* 116: 825, 1941.
3. Levine, P., Burnham, L., Katzin, E. M., and Vogel, P.: *AM. J. OBST. & GYNEC.* 42: 925, 1941.
4. Levine, P.: *New York State J. Med.* 42: 1928, 1942.
5. Race, R. R.: *Nature* 153: 771, 1944.
6. Wiener, A. S.: *Proc. Soc. Exper. Biol. & Med.* 56: 173, 1944.
7. Wiener, A. S.: *Arch. Path.* 32: 227, 1941.
8. Levine, P.: *Science* 96: 452, 1942.
9. Levine, P.: cited by Wiener: *Blood Groups and Transfusion*, ed. 3, Springfield, Ill., 1942, Charles C Thomas, pp. 253-254.
10. Levine, P.: *J. Pediat.* 23: 656, 1943.
11. Wiener, A. S.: *Science* 100: 595, 1944.
12. Race, R. R.: *Nature* 153: 772, 1944.
13. Murray, J.: *Nature* 154: 701, 1944.
14. Race, R. R., et al.: *Nature* 152: 563, 1943.
15. Wiener, A. S., and Sonn, E. B.: *J. Immunol.* 47: 461, 1943.
16. Levine, P., and Wong, H.: *AM. J. OBST. & GYNEC.* 45: 832, 1943.
17. Levine, P.: *Yearbook of Pathology and Immunology*, 1941, p. 508.
18. Race, R. R., and Taylor, G. L.: *Nature* 152: 300, 1943.
19. Levine, P.: *Arch. Path.* 37: 83, 1944.
20. Levine, P.: Unpublished data.*
21. Levine, P.: *J. Hered.* 34: 71, 1943.
22. Levine, P.: *West. J. Surg.* 50: 468, 1942.
23. Levine, P.: *Am. J. Clin. Path.* 11: 898, 1942.
24. Yannet, H.: *Bull. New York Acad. Med.* 20: 562, 1944.
25. Snyder, L. H., Schonfeld, M.D., and Offerman, E. M.: *J. Hered.* 36: 9, 1945.
26. Levine, P.: *Human Fertil.* 9: 68, 1944.
27. Mayes, H. W.: *AM. J. OBST. & GYNEC.* 48: 36, 1944.

*In twenty-three cases of erythroblastosis fetalis in the first born, a transfusion history was obtained in sixteen instances. The chances for fetal death in the first born are ten times greater in previously transfused mothers than in the control group not transfused.

Department of Reviews and Abstracts

Review of New Books

Obstetrics and Gynecology

Dr. McCormick's monograph on the Pathology of Labor, the Puerperium, and the Newborn¹ is an outgrowth of his lectures at Indiana University. Although the author states that he sets forth only the essentials of present-day obstetric thought, the book is in no sense a compendium or synopsis, but gives a really fine discussion of the abnormalities which may complicate the two phases of the reproductive process. Under abnormal labor one finds an excellent discussion of the faults of the powers, passages, and passenger. While the author describes the mechanism and treatment of labor in contracted pelves, he does not mention the classification of Caldwell and Moloy. Although the teaching is undoubtedly largely personal, one enjoys the insertion of treatment recommended by heads of other institutions, which, with their bibliographic references, are inserted appropriately in the text. The discussion of obstetric injuries stresses the prophylaxis and avoidance of such complications.

Obstetric operations are discussed under twenty-four headings, and the advantages and disadvantages of many alternate procedures are succinctly phrased. The illustrations in this part of the book have been well chosen. The types, choice, and performance of cesarean section is well correlated with the previous discussion on labor in the contracted pelvis. The postoperative treatment of obstetric operations is detailed. The pathology of the puerperium comprises largely a discussion of the various types of puerperal infections and puerperal hemorrhage. The author discussed the various complications which may occur in the use of the sulfonamides and presents the most recent ideas on the use of penicillin. He recommends frequent blood transfusions in combination with either of the two agents mentioned. Nowhere in his discussion of blood transfusion as a therapeutic measure has the possibility of an Rh factor reaction been mentioned, although the subject of isoimmunization is mentioned in a short section on the pathology of the newborn. The book closes with an appendix on obstetric analgesia, several sections of which are presented by guest contributors. The author comments toward the end of this section, that continuous caudal analgesia is not suitable for general use. The subject is covered completely yet with a clarity and a conciseness which should accord a popular reception for the book.

PHILIP F. WILLIAMS.

The Abortion Problem,² proceedings of a conference held under the auspices of the National Committee on Maternal Health in June of 1942, covers many aspects of this involved subject. The Conference was attended by many leaders in investigative and clinical medicine as well as by members of the legal profession.

The main subjects discussed fall under four headings: magnitude of the abortion problem; spontaneous abortion and its prevention; social, moral, and economic causes and control of abortion; the control of the abortion problem.

¹*Pathology of Labor, the Puerperium, and the Newborn.* By Charles O. McCormick, A.B., M.D., F.A.C.S., Clinical Professor of Obstetrics, Indiana University School of Medicine; Consulting Obstetrician to William H. Coleman Hospital for Women, Indianapolis City Hospital, and Sunny Side Sanitarium. 382 pages. 191 illustrations. Including ten in color. The C. V. Mosby Company, St. Louis. 1944.

²*The Abortion Problem.* Proceedings of the Conference Held Under the Auspices of the National Committee on Maternal Health, Inc., at the New York Academy of Medicine, June 19 and 20, 1942. Howard C. Taylor, Jr., M.D., Conference Chairman. 182 pages. Published for the National Committee on Maternal Health, Inc., by The Williams & Wilkins Company, Baltimore. 1944.

This report, which covers so many aspects and angles, makes evident the complexities of the subject, but as could be expected, offers little help for either combating spontaneous abortion or suppressing illegal abortion.

R. T. FRANK.

This volume is a splendid presentation of the essential information with respect to *Control of Pain in Childbirth*.³ The book itself is excellently done on fine paper and easily readable print. The illustrations are profuse, informative, and well made. The comprehensive explanation of the anatomy involved in the use of caudal anesthesia presented together with a discussion of the neurological features should be read by every obstetrician and anesthetist. It is due to the authors' concentration on a particular subject in the field of anesthesiology that advances in this specialty are made so rapidly. Several physicians have contributed directly or indirectly to some of the material presented. Without a doubt the coverage of the subject in this book is the most complete that has yet appeared.

JOHN S. LUNDY.

The questions *The Woman Asks the Doctor*,⁴ most frequently concerning the genital tract, are answered by Dr. Novak in a series of eleven chapters on the various aspects of female anatomy and menstrual and reproductive physiology. In thoroughly scientific yet easily understood diction the book traverses the whole subject of femininity from embryologic origin through the menopause, and there are additional chapters on such disturbing pathologic conditions as disorders of menstruation, malignancy, and birth control. The frank and simple manner of presentation should occasion a very frequent recommendation of this book to those patients who seem to be interested in knowing more concerning their "femaleness."

PHILIP F. WILLIAMS.

The fact that a great majority of ailments encountered in gynecologic practice are the result of infection or trauma contracted during labor has influenced the authors of this important volume, prominent teachers of the British Isles, to combine the subject of obstetrics and gynecology in one text. The present fourth edition, *A Combined Textbook of Obstetrics and Gynecology*, which is edited by Munro Kerr,⁵ follows closely the arrangement of previous editions.

The editor has joined to his list of authors several contributors on specific topics. The section on Anesthesia has been written by Dr. Landau, who does not consider paracervical block sufficiently reliable for routine use. The chapter on sterility contributed by Mr. Green-Armytage is excellent, and in this edition for the first time contraception is discussed. The presentation of radiology by Mr. G. Jackson Wilson follows current practices in the United States. The use of the sulfonamides in gonorrheal and other pelvic infections is detailed. Although obstetric surgery is quite fully presented, the details of gynecologic operative technique are not given. It is the feeling of the authors that the latter is not germane to the teaching of medical undergraduates. This book is again highly recommended for medical students or general practitioners.

PHILIP F. WILLIAMS.

Dr. Greenhill's review of the literature in *The 1944 Year Book of Obstetrics and Gynecology*⁶ provides a ready reference volume in which one will find a well-selected

³*Control of Pain in Childbirth*. By Clifford B. Lull, M.D., F.A.C.S., Clinical Professor of Obstetrics, Jefferson Medical College; Assistant Director, Philadelphia Lying-In Unit, Pennsylvania Hospital, and Robert A. Hingson, M.D., Surgeon, U. S. Public Health Service; Director, Postgraduate Medical Course, Philadelphia Lying-In Unit, Pennsylvania Hospital. 356 pages, 132 illustrations. J. B. Lippincott Company, Philadelphia, London and Montreal. 1944.

⁴*The Woman Asks the Doctor*. By Emil Novak, M.D., F.A.C.S., Honorary D.Sc. (Dublin), Associate in Gynecology, Johns Hopkins Medical School; Gynecologist, Bon Secours and St. Agnes Hospitals. Second edition. 120 pages. 11 illustrations. The Williams & Wilkins Company, Baltimore. 1944.

⁵*Combined Textbook of Obstetrics and Gynecology*. For Students and Medical Practitioners. Revised by J. M. Munro Kerr, LL.D., M.D., F.R.F.P. (Glas.), F.R.C.O.G., Professor Emeritus of Midwifery, Glasgow University; formerly Obstetric Surgeon, Glasgow Royal Maternity and Women's Hospital. Fourth edition. 1,169 pages. 511 illustrations, some in color. The Williams & Wilkins Company, Baltimore. 1944.

⁶*The 1944 Year Book of Obstetrics and Gynecology*. Edited by J. P. Greenhill, B.D., M.D., F.A.C.S., Professor of Gynecology, Cook County Graduate School of Medicine. The Year Book Publishers, Chicago. 1945.

discussion of recent articles dealing with the principle topics of the two specialties. The editor has included a great deal of material on continuous caudal analgesia, but states in his comment at the end of the section that he is even more convinced than he was a year ago that continuous caudal analgesia will not become part of our obstetric armamentarium. There are many references to the present status of the sulfonamide group of drugs in both puerperal and nonpuerperal pelvic infections. There is a long review of the literature on endocrinology, and the editor notes the narrowing indications for the use of various hormones. The few articles which have appeared on penicillin are reviewed and its efficacy is compared with that of the sulfonamides. The volume offers an opportunity for a rapid review of the present status of research and therapy in these specialties.

PHILIP F. WILLIAMS.

An elaborate monograph on **Leukoplakia of the Vulva** is published by Octaviano Alves De Lima Filho.⁷ This is based on nine cases of leukoplakia as well as leukoplakic kraurosis seen by the author in 1,186 patients, which is a percentage of 0.67 per cent. He believes that leukoplakia shows a marked preference for the white race. Syphilis and estrogenic insufficiency appear to play an etiological role. The author mentioned the many theories and hypotheses which have been proposed, covering such possibilities as allergy, avitaminosis, etc. There are a number of beautiful gross colored photographs as well as many illustrations of microscopic sections, and a rather full consideration of the literature. In spite of its completeness and accuracy, the monograph presents nothing new.

R. T. FRANK.

Endocrinology

Endocrinology of Woman by Hamblen⁸ may be considered a second edition, entirely rewritten, of his *Endocrine Gynecology* which appeared five years ago. The book is large, ambitiously planned, well executed, requiring an immense amount of garnering of the literature, codification, and interpretation. Its fifty-two chapters reflect the large clinical and thorough laboratory experience of the author.

Eighty-five pages are devoted to consideration of the separate endocrine glands, their embryology, anatomy, chemistry, physiology, etc. The testes are included. Although brief, the presentation is accurate, modern, and up to date. The chemistry is clear and understandable. Part two deals with the female sex function from the fetus through the climacteric. I know of no other book which contains as ample, clear-cut, and well-collated a summary of our knowledge of this phase of the subject in such short compass.

Diagnostic methods are considered in the third section. This includes anthropometric, pelvic, histologic (biopsy, spreads), bacteriologic, chemical, and hormonal investigations and methods, briefly, but in detail. Accompanying tables and charts are valuable for ready reference. Part four covers functional disorders of the endocrine glands. The chapter on adrenal diseases is especially satisfactory. In functional ovarian disease, Hamblen describes "hypoprogesterinism" which, in my opinion, does not as yet warrant classification as a disorder.

Part five deals with endocrinology applied to gynecologic diseases. It includes abnormal skeletal growth, abnormal sex differentiation, obesity, and leanness. Uterine bleeding, pregnancy complications, dysmenorrhea, sterility, the climacteric. In addition, dermatologic abnormalities, breast and other cyclic disturbances are described. The classification of uterine bleeding is too involved, its treatment too schematic.

This book can be used as a source for endocrine literature. Between the footnotes and chapter bibliographies, much ground is covered. The author has experience and entertains opinions which he does not hesitate to express. Occasionally I must differ with him categorically, as for instance when he declares that "the Friedman test has been found to be positive in many nonpregnant conditions," and that "the author believes

⁷**Leucoplasia Vulvar.** By Octaviano Alves de Lima Filho, Assistente efetivo da Clínica Ginecológica da Escola Paulista de Medicina. Laureado pela Academia Nacional de Medicina com o prêmio "Madame Durocher" em 1912. 240 pages. Livraria Atheneu—Jose Bernades, Sao Paulo, Brazil. 1944.

⁸**Endocrinology of Woman.** By E. C. Hamblen, B.S., M.D., F.A.C.S., Clinical Professor of Endocrinology and Associate Professor of Obstetrics and Gynecology, Duke University School of Medicine; Chief of the Endocrine Division and Endocrinologist, Duke Hospital, Durham, N. C. 571 pages. Charles C Thomas, Springfield, Ill. 1945.

the Aschheim-Zondek test is more reliable" Also that "the comb response of the baby chick . . . [is] too unreliable for assay use." All in all, however, this endocrinology is a valuable contribution, useful to both endocrinologist and gynecologist.

R. T. FRANK.

The fifth edition since 1933 of *Recent Advances in Endocrinology* by Cameron⁹ has appeared. In order to conserve space, it has been almost completely rewritten. In this edition, the clinical aspects have received greater emphasis. The literature is dealt with until the end of 1943. This volume differs from the so-called year books in that it gives access to the newer publications and discoveries, but does not describe them in a haphazard fashion. This is achieved by describing the history as well as the entire aspect of each subject taken up.

The chapter on the steroid hormones and related compounds is unusually detailed, clear, and satisfactory. The same may be said for the chapter on Cushing's disease and adrenocortical syndromes. This does not signify that the other chapters are not satisfactory. On the contrary, this book makes very interesting and instructive reading and is well worth while for those who try to keep abreast of newer discoveries in a general fashion, and is sufficiently detailed to interest those who specialize in the subject.

R. T. FRANK.

Von Wattenwyl¹⁰ has produced a faultlessly gotten up monograph on the effect of prolonged application of estrogens. The main theme is the implantation of tablets of natural and synthetic estrogens in guinea pigs and other rodents. The material is not very extensive but the methods are careful and well executed. In the main, these experiments are repetition and confirmation of the work performed by others, particularly by Lipschitz of Chile. The observation that prolonged treatment with estrogens caused transient alopecia is new.

This monograph serves as an excellent review of all phases of the subject dealt in.

R. T. FRANK.

Miscellaneous

Outline of the Amino Acids and Proteins,¹¹ edited by Sahyun, and with twelve additional contributors, some engaged purely in research, others connected with research and industry, is a fascinating monograph. This book can be read, perhaps with a trifle of difficulty, by the average physician as well as the chemist. It covers the discovery of the individual amino acids, which really is a romantic chapter in research. The tremendous amount of work that has been put on this subject for the last one hundred years is beginning to give results. The formation of protein by linkage of the amino acids, their grouping according largely to physical properties, especially to solubilities, is taking more and more definite shape. The investigation of the simple proteins, such as the albumins, globulins, prolamines, histones, and protamines, is very definite. Less advanced, of course, is our knowledge of the conjugated proteins, that is, those combined with prosthetic groups of nonprotein nature. Some of the most important biologic compounds fall in this group, such as hemoglobin, coenzyme, yellow enzyme, and nucleoproteins, including the viruses. In this large group fall the chromoproteins, glycoprophosphoproteins, as well as the endocrine proteins. In the latter, we may put thyroglobulin, insulin, prolactin, covering those which have been obtained in crystalline form. In the study of the proteins, the size of the molecule, the surface films, the nature and effect of hydrolysis, the more successful and intricate syntheses are playing a greater role.

It is impossible in a review to give more than the barest idea of the tremendous amount of knowledge, some of it still in the hypothetical and borderline state, which

⁹*Recent Advances in Endocrinology*. By A. T. Cameron, M.A., D.Sc. (Edin.), F.R.I.C., F.R.S.C., Professor of Biochemistry, Faculty of Medicine, University of Manitoba; Biochemist, Winnipeg General Hospital. Fifth edition, with 73 figures, including three plates. 415 pages. The Blakiston Company, Philadelphia. 1945.

¹⁰*Tierexperimentelle Untersuchungen über die Wirkung langdauernder Follikelhormonapplikation und die Hormonale Tumorentstehung*. Von Dr. Hubert Von Wattenwyl, Privatdozent Oberarzt am Frauenspital Basel. 235 pages. Benno Schwabe & Co., Basel, Switzerland. 1944.

¹¹*Outline of the Amino Acids and Proteins*. Edited by Melville Sahyun, M.A., Ph.D., Vice-President and Director of Research, Frederick Stearns and Company, Detroit, Michigan. Contributing Authors: Henry B. Dull, William M. Cahill, Herbert E. Carter, David M. Greenberg, Michael Heidelberger, Irving R. Hooper, Carl L. A. Schmidt, C. F. Kade, Armand J. Quick, Melville Sahyun, Arthur H. Smith, Madelyn Womack, and Dean Laurence. 251 pages. Reinhold Publishing Corporation, New York. 1944.

will be found in its pages. This book is really illuminating to the physician who has not had the opportunity of following the rapid increase in knowledge. It is probably indispensable to the chemist, both the student and the practicing one.

R. T. FRANK.

Dr. Oberndorf has undertaken the fascinating task of presenting *The Psychiatric Novels of Oliver Wendell Holmes*,¹² in abridged form, with an introduction and with many annotations. He has succeeded in interesting a large audience as shown by the fact that since 1943 this book has undergone three printings.

It has been the fashion fairly recently to somewhat minimize the achievements of Oliver Wendell Holmes because of his flamboyance, his activities in political medicine, and his delight in personal advertisement. However, nobody can remove from him the immense credit of having discovered the contagiousness of "puerperal fever," and second, nobody can decry his uncanny insight into the psychological sphere as evidenced by the three novels which Dr. Oberndorf has abridged. *Elsie Venner* is a story of a schizophrenic. *The Guardian Angel* presents hysteria in a young girl. *A Mortal Antipathy* is a young man's morbid fear (gynophobia).

Oberndorf is fully justified in considering Holmes as a precursor of Freud. The novels were meant to show that there is no inherited guilt. Holmes realized that dreams are battles with ourselves, unconscious that we are our own antagonists. He likewise understood that automatic unconscious actions of the minds enter into the thought mechanism. He realized the force of childhood memories; the effect of sexual frustrations in producing physical symptoms. Oberndorf points out the salient factors that the casual, even the medical reader, might overlook. He emphasizes, for example, that all of the major characters lost their mothers before the age of two. His footnote annotations are modern keynotes to Holmes's text. This book makes delightful and instructive reading and should put *Elsie Venner* and *The Guardian Angel* particularly, into the reading of the younger generation who had been frightened off by Holmes's somewhat prolix style which has been removed by the abridgement.

R. T. FRANK.

Criep has written *Essentials of Allergy*¹³ as the fifth in the series of Lippincott's *Essentials*. The book is designed for both the practitioner and the medical student as a working manual in outline form. The subject is certainly important because 10 per cent of the population suffers from major allergies and up to 50 per cent from minor allergies. The principles of immunology are carefully but briefly gone into, and then their clinical application is given. In each chapter there are many case histories and each chapter is concluded with a bibliography. A fairly complete dietary, designed to avoid certain foodstuff, is included, as well as many tables and good illustrations. This manual is well written, sound, and should prove of real use, particularly to those who are interested chiefly in direct clinical application.

R. T. FRANK.

The fourth edition of Kolmer and Boerner's *Approved Laboratory Technic*¹⁴ appears after an interval of four years. Thirty collaborators were enlisted to cover the enormous amount of detail which today is embraced by the term of clinical pathology. The contents does not lend itself to detailed review. It includes not only clinical pathology

¹²*The Psychiatric Novels of Oliver Wendell Holmes*. Abridgment, Introduction, and Annotations by Clarence P. Oberndorf, M.D., Clinical Professor of Psychiatry, Columbia University. 268 pages. Columbia University Press, New York. 1943.

¹³*Essentials of Allergy*. By Leo H. Criep, M.D., Assistant Professor of Medicine and Lecturer in Immunology, School of Medicine, University of Pittsburgh, Diplomate in Internal Medicine (1937), Fellow of the American Academy of Allergy, Chairman, Department of Medicine, Montefiore Hospital and Senior Staff in Medicine, Presbyterian and Passavant Hospitals, Pittsburgh, Consultant in Allergy to the Medical Service of the U. S. Veterans Administration. With a Foreword by Robert A. Cooke, M.D., Chairman, Committee on Education, American Academy of Allergy. 42 illustrations in black and white and 1 plate in full color. 381 pages. J. B. Lippincott Company, Philadelphia. 1945.

¹⁴*Approved Laboratory Technic*. Clinical Pathological, Bacteriological, Mycological, Virological, Parasitological, Serological, Biochemical and Histological. By John A. Kolmer, M.S., M.D., Dr. P. H., ScD., LL.D., L.H.D., F.A.C.P., Professor of Medicine in the School of Medicine and the School of Dentistry, Temple University; Director of the Research Institute of Cutaneous Medicine; Formerly Professor of Pathology and Bacteriology, Graduate School of Medicine, University of Pennsylvania, and Fred Boerner, V.M.D., Associate Professor of Clinical Bacteriology, Graduate School of Medicine and Assistant Professor of Bacteriology, School of Medicine, University of Pennsylvania; Bacteriologist, Graduate Hospital, Philadelphia. Fourth edition. 1,017 pages. D. Appleton-Century Company, Inc., New York. 1945.

but also bacteriology, mycology, virology, parasitology, serology, biochemical and histological techniques. A section on hormonology—pregnancy, estrin, and gonadotropic tests—has been added. It is rather sketchy. The determination of penicillin and the sensitivity of bacteria to this drug are included. Many additions and changes have been made which bring the useful and important book fully up to date.

R. T. FRANK.

This is an objective study of the relationship of the basic sex differences to the behavior patterns in men and women.¹⁵ In making this study of the fundamental differences in thought, temperament and activities of the two sexes, Dr. Scheinfeld has investigated many theories, has exhaustively analyzed the literature, and has consulted experts in the various problems of this study. Beginning with embryologic formation, he proceeds through the development of infancy and adolescence, and discusses the modifying influence of physical and sexual factors, in the transition from puberty to maturity. The psychological development, the variances in sex attitudes, and the influence of the divisions of labor in the male and female bring out many points of interest. Discussing relative achievement and genius in the two sexes, he portrays with considerable finesse the inhibitory barriers which formerly restrained equality in various fields. This chapter is an excellent study of the career woman.

The book is extensively documented, with many tables and illustrations and, while the author's philosophy is somewhat extended, the book is interesting reading on the psychological influence of the biological factors on the character of sexes.

PHILIP F. WILLIAMS.

This book *Psychology of Women* by Dr. Deutsch¹⁶ is offered as the first volume of a two-part study. The present volume carries the process of development of the female psyche across the threshold of maturity. Dr. Deutsch states that the second part will deal with the salient life phases of adult womanhood.

This psychoanalytic interpretation is a clinical study of why women act a certain way, and is an attempt to explain the normal psychology of women and their conflicts. The text is offered in ten chapters, and discusses three distinct although related themes. The early chapters deal with the development of the psychology of a young girl, a development that is closely associated with menstruation. Dr. Deutsch regards this period as the one in which the foundations of feminine personality are definitely formed. In succeeding chapters she discusses the three essential traits of femininity: narcissism, passivity, and masochism. These essential traits are thoroughly amplified by clinical instances. The variances from such essential traits are discussed in relation to the factors, physiologic, sexual, or social which produce either the nonfeminine or, further, the masculine type of woman. Those who are interested in the various abnormal types of psychological development or behavior in women will find much of value in this text.

PHILIP F. WILLIAMS.

Dr. Groves, in *The American Woman*,¹⁷ discusses woman's changing status in the United States and stresses her advance toward equality with men. From a background of woman's earlier position and her situation in Europe prior to the seventeenth century, he develops the changing cultural background of woman. As to the American woman, he portrays her position in colonial days, and her life and work on the frontier in the expansion of our domestic economy. The modifying geographic influence on women in the North and South and of the continued expansion of our country to the West forms a large section of the text, and gives a graphic picture of the social and political changes in the various parts of our country during the period from the Revolution to the Civil War. He discusses the American woman as a single unit in the period after the Civil War, with reference especially to her educationally improved position and her beginning

¹⁵*Women and Men*. By Amram Scheinfeld. 402 pages. Harcourt, Brace and Company, Inc., New York. 1944.

¹⁶*The Psychology of Women*. A Psychoanalytic Interpretation. By Helene Deutsch, M.D., Associate Psychiatrist, Massachusetts General Hospital Lecturer, Boston Psychoanalytic Institute. Foreword by Stanley Cobb, M.D., Bullard Professor of Neuropathology, Harvard University. Volume One. 386 pages. Grune & Stratton, Inc., New York. 1944.

¹⁷*The American Woman*. The Feminine Side of a Masculine Civilization. By Ernest R. Groves, Professor of Sociology, University of North Carolina. Second edition. 424 pages. Emerson Books, Inc., New York. 1944.

participation in industry. Discussion of the past four decades portrays woman's part and influence in many social changes of this period, such as suffrage, the prohibition question, child welfare, and the employment of women and children in industry. The latter portion of the book discusses the changing status of women just prior to and during our war years, as well as her participation in World War II. The book is an interesting and complete contribution to the life and problems of the American woman and presents many implications of interest to those who are concerned in her health.

PHILIP F. WILLIAMS.

This small volume *Medical Uses of Soap*¹⁸ is a collection of articles on the chemistry, manufacture, and the usual and the abnormal and the therapeutic effects of soap on normal and diseased skin. There are chapters regarding the use of soap on the hair and in shaving and a consideration of its use in prophylaxis as well as therapy of various diseases. There is much in the book which could be useful to the industrial surgeon, dermatologist, or the family physician.

PHILIP F. WILLIAMS.

¹⁸*Medical Uses of Soap. A Symposium.* Edited by Morris Fishbein, M.D. 178 pages. J. B. Lippincott Company, Philadelphia. 1945.

Correspondence

Relaxation of Constriction Ring With Adrenalin Chloride in a Cesarean Section Under Spinal Anesthesia

To the Editor:

In November, 1943, under *Correspondence* in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*, I reported a case "Relaxation of Bandl's Contraction Ring With Adrenalin Chloride" in a cesarean section under spinal anesthesia. This anesthesia being uniform in its effect ruled out the fact that the deepening anesthesia (Brown and Wilder, April, 1943, *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*) caused the relaxation rather than the adrenalin chloride.

Within the past year I had another opportunity to observe the same phenomenon in the case reported below. The operator and his assistant were both skeptical, so no comment was made by me when the relaxation began to occur, but when it did occur they admitted it to be a fact. In this case disproportion made a cesarean section necessary, but if adrenalin chloride (unless otherwise contraindicated) was used in every case of even suspected constriction ring, it would cause no harm and might prevent many unnecessary cesarean sections. Two cases of anything are a small number to report but planned experiments could not have been more conclusive proof of the ability of adrenalin chloride to relax a constriction ring.

A 27-year-old Negro woman pregnant for the first time was admitted to the hospital in hard labor with the history of having been in labor for the past five days. The membranes were said to have ruptured three days before. X-ray showed a large baby and a small pelvis.

With a living baby, no cervical dilatation, the patient in good condition, and definite cephalopelvic disproportion, a cesarean section was considered indicated. A single shot spinal with ephedrine was the anesthesia used. When the uterus was exposed, the constriction ring was very prominent in the upper segment of the uterus. Five minims of adrenalin chloride were given subcutaneously and within four minutes relaxation had begun and was apparently complete within another minute. A 12-pound living male infant was delivered. The constriction ring was about the baby's hips and was tight enough to cause an ecchymotic ring just above the hips and back (a Negro baby is light in color).

The mother's recovery was uneventful and both left the hospital in good condition on the fifteenth day.

ADAM T. THORP, M.D.

ROCKY MOUNT, N. C.

MARCH 20, 1945.

Items

American Board of Obstetrics and Gynecology

Examinations

The general oral and pathology examinations (Part II) for all candidates will be conducted at Atlantic City, New Jersey, by the entire Board from Wednesday, June 13, through Tuesday, June 19, 1945. The Hotel Shelburne in Atlantic City will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel.

Candidates for *re-examination* in Part II must make written application to the Secretary's Office not later than April 15, 1945.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

Deferment without time penalty under a waiver of our published regulations applying to civilian candidates, will be granted if a candidate in Service finds it impossible to proceed with the examinations of the Board.

Applications are now being received for the 1946 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS, M.D.

Announcement

In compliance with the directives imposed by the War Production Board limiting the amount of paper consumed in the production of this JOURNAL, the publishers find it necessary to change the format. As soon as these restrictions are lifted the original format will be restored. Even though the number of pages has been reduced, the actual content of the JOURNAL has not been decreased to any appreciable extent.

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